Red Cell Distribution Width as Outcome Predictor in Organophosphate Poisoning

Dissertation submitted in partial fulfillment of the

Requirement for the award of the Degree of

DOCTOR OF MEDICINE

BRANCH I - GENERAL MEDICINE

APRIL 2019

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

CERTIFICATE FROM THE DEAN

This is to certify that the dissertation entitled "**Red Cell Distribution Width as Outcome Predictor in Organophosphate Poisoning** " is the bonafide work of **DR. S. ARUN PRANAAV** in partial fulfillment of the university regulations of the Tamil Nadu Dr. M.G.R. Medical University, Chennai, for **M.D General Medicine Branch I** examination to be held in April 2019.

Dr. D.MARUTHUPANDIAN M.S., FAIS.,FICS

THE DEAN, MADURAI MEDICAL COLLEGE,

GOVERNMENT RAJAJI HOSPITAL,

MADURAI.

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Dr. V. T. PREM KUMAR, M.D.,

PROFESSOR AND HOD,

DEPARTMENT OF GENERAL MEDICINE,

GOVERNMENT RAJAJI HOSPITAL ,

MADURAI MEDICAL COLLEGE, MADURAI

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Dr. C. DHARMARAJ, M.D(GM)., D.CH.,

PROFESSOR OF MEDICINE,

DEPARTMENT OF GENERAL MEDICINE,

GOVERNMENT RAJAJI HOSPITAL,

MADURAI MEDICAL COLLEGE,

MADURAI.

DECLARATION

I, Dr. S. Arun Pranaav declare that, I carried out this work on "**Red Cell Distribution Width as Outcome Predictor in Organophosphate Poisoning**" at the Department of General Medicine, Government Rajaji Hospital, Madurai under the guidance of **Dr. C.DHARMARAJ, M.D(GM)., D.CH.,** Professor, Department of General Medicine, Madurai medical college,Madurai.

I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, Diploma to any other University, Board either in India or abroad.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. MedicalUniversity, Chennai in partial fulfillment of the rules and regulations for theaward of **Doctor of Medicine (M.D.), General Medicine Branch-I**,examination to be held in **April 2018.**

Place: Madurai
Date:

Dr. S.ARUN PRANAAV

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ABSTRACT

Abstract:

Introduction:

Suicidal poisoning by OPC is however a major clinical and public health concern Red cell distribution width measures variability in RBC size. That means it reflects anisocytosis. It can easily be assessed in a complete blood count. It is found to be elevated heart failure, acute coronary syndromes and pancreatitis.

In organophosphate poisoning too there can be acute inflammation and oxidative stress. This too may cause a change in structure and size of RBC. So there is an expected increase in red cell distribution width. The level of elevation is associated with the level of inflammation and oxidative stress. Hence RDW can be assessed as a prognostic marker in organophosphate poisoning

Objectives:

To Investigate the relation between Red cell distribution width and final outcome in patients with organophosphate poisoning

Materials and Methods:

The study will be conducted on 200 patients admitted to Government Rajaji Hospital & Madurai Medical College with history of organophosphate poisoning during the study period

We included patients with clinical history of ingestion of OPC poison between age 13- 60 yrs, did initial clinical assessment, serum pseudocholinesterase and RDW

INTRODUCTION

Title:
Red Cell Distribution Width as Outcome Predictor in Organophosphate Posioning

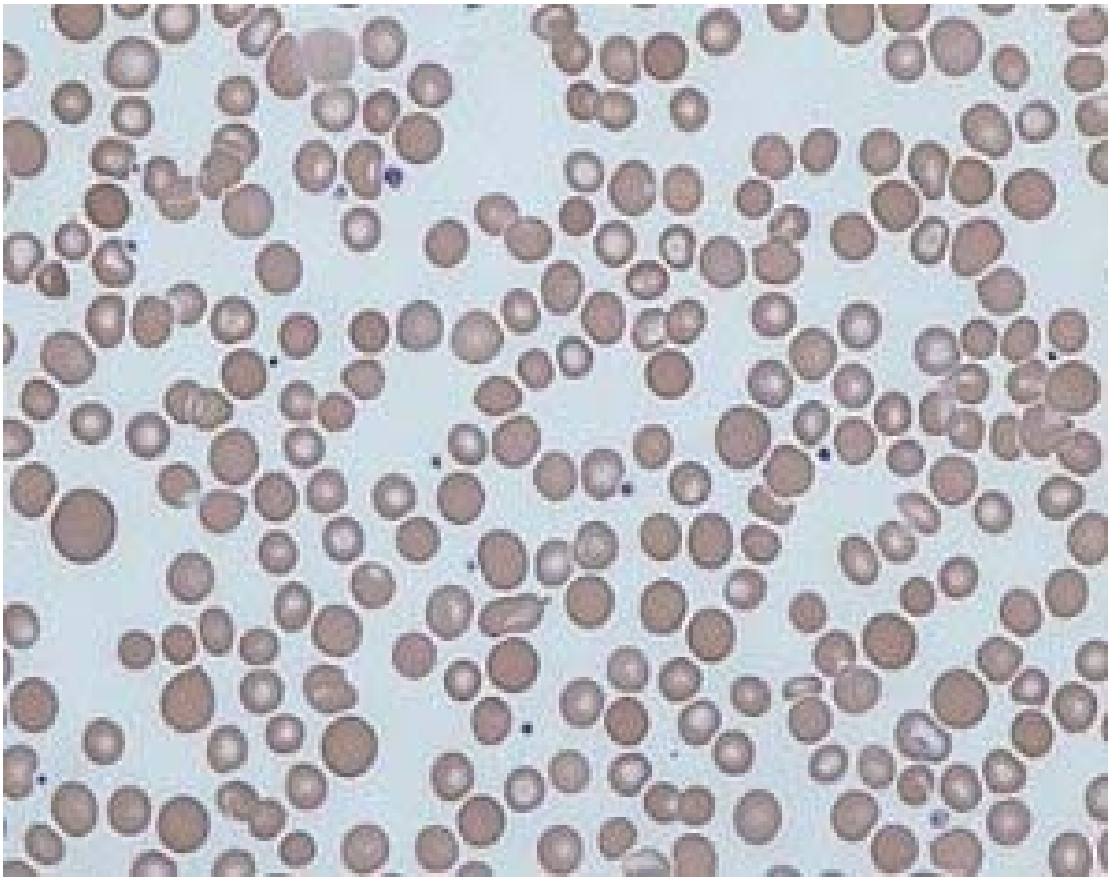
Suicidal poisoning by OPC is however a major clinical and public health concern Red cell distribution width measures variability in RBC size. That means it reflects anisocytosis. It can easily be assessed in a complete blood count. It is found to be elevated heart failure, acute coronary syndromes and pancreatitis.

OPC poisoning causes generation of reactive oxygen species due to its redox cycling activity, thereby releasing Superoxide dismutase which damages the phospholipid membrane of RBC's

Since RBCs have no nucleus and mitochondria they are affected first along with other hematological changes like dendritic cells inhibiton, leukocytosis

Damaged RBC’s show increased anisocytosis with the condition aggravated due to hypoxia and susbsequent denaturation of Heme compound

Peripheral smear showing Anisocytosis



OBJECTIVES

Objectives:

To investigate the relation between Red cell distribution width and final outcome in patients with organophosphate poisoning

REVIEW OF LITERATURE

REVIEW OF LITERATURE:

Organophosphate (OP) compounds are a diverse group of chemicals used in both domestic and industrial settings. Examples of organophosphates include the following:

Insecticides – Malathion, parathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion

Nerve gases – Soman, sarin, tabun, VX

Ophthalmic agents – Echothiophate, isoflurophate

Antihelmintics – Trichlorfon

Herbicides – Tribufos (DEF), merphos

Industrial chemical (plasticizer) – Tricresyl phosphate

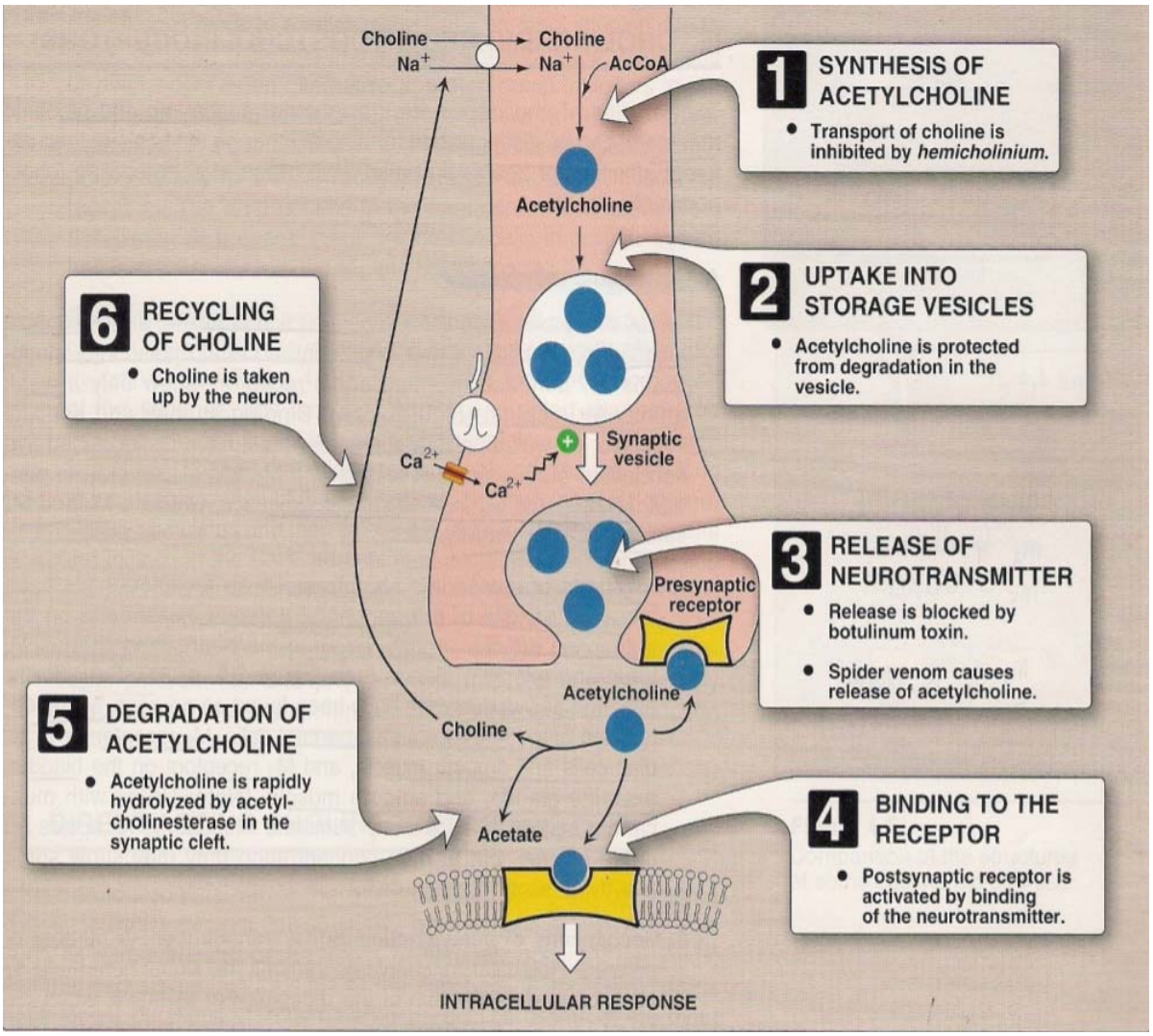
Thus, organophosphate toxicity can result from household or occupational exposure, military or terrorist action, or iatrogenic mishap. Exposure to organophosphates is also possible via intentional or unintentional

contamination of food sources. Although no clinical effects of chronic, low-level organophosphate exposure from a food source have been shown, advancements in risk assessment and preparedness are ongoing.

Mechanism of OPC action include

- OP compounds phosphonylate the active site of acetylcholinesterase (AChE), inactivating the enzyme leading to the accumulation of acetylcholine (ACh) in cholinergic synapses
- Spontaneous hydrolysis of the OP-enzyme complex allows reactivation of the enzyme.
- AChE-dimethyl OP complex spontaneously reactivate in less than one day

- AChE-diethyl OP complex may take several days and reinhibition of the newly activated enzyme can occur significantly
- spontaneous reactivation can be hastened by adding nucleophilic reagents like oximes, liberating more active enzymes.



Signs and symptoms of organophosphate poisoning can be divided into three broad categories: (1) muscarinic effects, (2) nicotinic effects, and (3) central nervous system (CNS) effects. Also classified as

1. Acute cholinergic syndrome (most common)

2. Sub acute proximal weakness (Intermediate syndrome)
3. Organophosphate induced delayed neuropathy (OPIDN)
4. Chronic organophosphate induced neuropsychiatric disorder (COPIND)

Acute cholinergic crisis

Muscarinic effects:

- Cardiovascular - Bradycardia, hypotension
- Respiratory - Rhinorrhea, bronchorrhea, bronchospasm, cough,severe respiratory distress
- Gastrointestinal - Hypersalivation, nausea and vomiting, abdominal pain, diarrhea, fecal incontinence
- Genitourinary - Incontinence
- Ocular - Blurred vision, miosis
- Glands - Increased lacrimation, diaphoresis

Nicotinic effect:

- muscle fasciculations
- cramping
- weakness
- diaphragmatic failure
- hypertension
- tachycardia
- mydriasis
- pallor

CNS effects:

- Anxiety
- Emotional lability
- Restlessness

- Confusion
- Ataxia
- Tremors
- Seizures
- Coma

Intermediate syndrome

- usually occurs 24 to 96 hours after the ingestion of an OP compound
- after an initial cholinergic crisis but before the expected onset of delayed polyneuropathy.
- Approximately 10-40% of patients treated for acute poisoning develop this illness.
- characterized by prominent weakness of neck flexors, muscles of respiration and proximal limb muscles.

- Mostly seen with fenthion, dimethoate and monocrotophos,
- muscle weakness may last up to 5-14 days, the condition regresses slowly if respiratory support is available.
- exact pathogenesis is unclear, the proposed mechanisms include persistent inhibition of AChE leading to functional paralysis of neuromuscular transmission, muscle necrosis, and oxidative free radical damage to the receptors

Organophosphate toxicity is a clinical diagnosis. Confirmation of organophosphate poisoning is based on the measurement of cholinesterase activity; but typically, these results are not readily available.

RBC ACETYLCHOLINESTERASE

- Direct measurement of RBC acetylcholinesterase (RBC AChE) activity provides the measure of the degree of toxicity
- The test is not usually available.

Plasma (Or Pseudo) Cholinesterase Activity

- is more easily performed
- does not correlate well with severity of poisoning
- should not be used to guide therapy.

AChE and PChE activity can fall to about 80% of normal before any symptoms occur and drop to 40% of normal before the symptoms become severe.

Biochemical Grading of Severity of Poisoning:

Red cell cholinesterase activity (% normal) Grade

- 20-50% Mild
- 10-20% Moderate
- <10% Severe

RED CELL ACETYLCHOLINESTERASE ACTIVITY

- Major disadvantage: Reactions between AChE, OP compounds and Oximes will continue if blood sample left at room temperature
- Samples must be diluted and cooled immediately
- Dilute by a factor of 20 by mixing 200 µL of sample into EDTA tube with 4 mL of cold saline & Freeze sample at -20 ˚C within 5 min

- Treatment begins with decontamination. Rapid initial assessment of airways, breathing, and circulation is essential.
- Comatose or vomiting patients should be kept in lateral, preferably head down position with neck extension to reduce the risk of aspiration.
- airway should be secured with proper positioning, placement of Guedel’s airway or with endotracheal intubation. Frequent suctioning is needed
- Oxygen used liberally to reduce the potiental problem of dysarrythmias
- Clothes should be removed and the skin vigorously washed with soap and water.

- Gastric lavage may help to reduce the absorption of the ingested poison and should be considered in patients presenting within 1-2 hours of ingestion of poison.
- Risks of gastric lavage include aspiration,hypoxia, and laryngeal spasm.

The mainstays of pharmacological therapy include atropine, pralidoxime (2-PAM), and benzodiazepines (eg, diazepam). Initial management must focus on adequate use of atropine -

INCREMENTAL DOSE

- 1.8 to 3.0 mg Atropine by IV
- Repeat the dose every 5 min interval doubling the dose each time to point of atropinisation
- Followed by 10-20% of total dose required as infusion per hour

BOLUS DOSE

- 2-5 mg Atropine every 10- 15 min till atropinisation
- Followed by maintenance using reduced doses or

increasing time duration between doses

End point of Atropinisation :

- Clear chest on auscultation with resolution of

bronchorrhea

- HR>80/min
- SBP>80 mm Hg
- Dry axilla
- Pupils >2mm in diameter
- Tachycardia not a contra-indication to Atropine
- Severe hypotension might benefit from Vasopressors
- Value of vasopressor Vs high dose atropine is not clear.

ATROPINE Vs GLYCOPYRROLATE

- Main adverse of Atropine – anti cholinergic delerium
- Glycopyrrolate - poor CNS penetration
- Ineffective in countering coma, reduced respiration.
- RCT showed no significant difference in mortality or ventilation rates
- Atropine will remain the anti-muscarinic agent of choice.

Characteristics of OXIMES are

- Ability to reverse AChE inhibition with oximes varies with pesticide ingested
- Diethyl OP compounds: effectively reactivated (t1/2 : 33 h) Dimethyl OP compounds: respond poorly (t1/2 : 3 h)
- Difference due to variation in speed of aging induced by different pesticides.

- Oximes not useful for late presentation of dimethyl OPC and large consumption of OPC (re-inhibits reactivated enzymes)

Cause of Death in OPC poisoning

1. Immediate death:

– Seizures.

– Complex ventricular arrhythmias.

2. Death within 24 hours:

– Acute cholinergic crisis in untreated severe case - Respiratory failure.

3. Death within 10 days of poisoning:

– Intermediate syndrome.

4. Late death:

– Secondary to ventricular arrhythmias, including Torsades de Pointes, which may occur up to 15 days after acute intoxication.

FAT SOLUBILITY AND HALF LIFE

- Fat soluable thionate OPCs (Fenthion) distribute in large amounts to fat stores after absorption
- Reduced peak concentration and mild early cholinergic features
- Subsequent slow distribution and activation - recurrent cholinergic features lasting days or weeks
- IMS common
- Oximes beneficial for many days
- Fat solubility graded as Kow. Less than 1.0 – not fat soluble and more than 4.0 – highly fat soluable

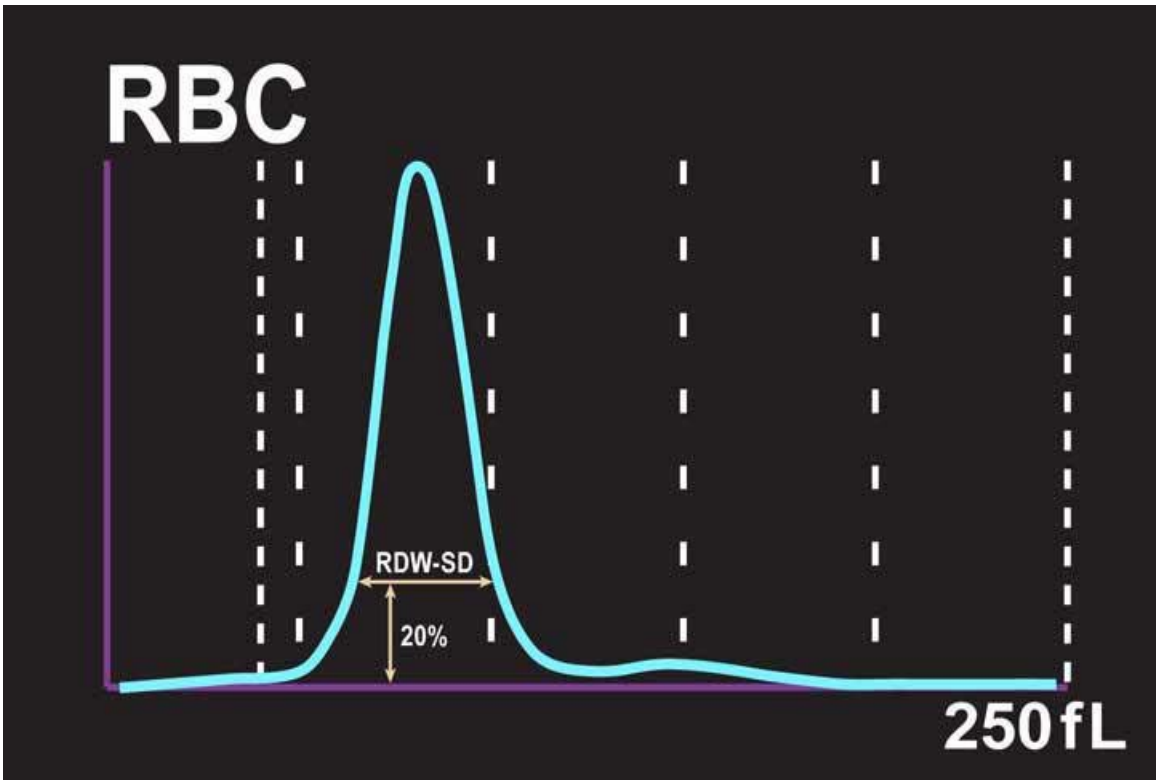
Red cell distribution width (RDW) is a red blood cell parameter that measures variability of red cell volume/size (anisocytosis). Depending on the types of hematology analyzer instruments, RDW can be reported statistically as coefficient of variation (CV) and/or standard deviation (SD), RDW-CV and/or RDW-SD, respectively.

RDW-SD (express in fL) is an actual measurement of the width of the RBC size distribution histogram and is measured by calculating the width (in fL) at the 20% height level of the RBC size distribution histogram. This parameter is therefore not influenced by the average RBC size (mean corpuscular volume, MCV).

RDW-CV (express in %) is calculated from standard deviation and MCV as follows

- RDW-CV (%) = 1 standard deviation of RBC volume/MCV x 100%

Of note, since RDW-CV is mathematically derived from MCV, it is therefore affected by the average RBC size (MCV).



Determination of RDW-SD measurement. In this example, RDW-SD is 38.2 fL.

RDW can be used as a guidance for flagging samples that may need manual peripheral blood smear examination, since elevated RDW may indicate red cell fragmentation, agglutination, or dimorphic red blood cell populations.

RDW has also been associated with a poorprognosis for other diseases and conditions, including stroke,community-acquired pneumonia (CAP), pulmonary embolism, chronicobstructive pulmonary disease (COPD), septic shock, and acutepancreatitis

Zerrin Defne Dundar et al did a study on total of 72 patients who ingested opi poison. Mechanically ventilated patients had significantly higher leukocyte counts and

RDWlevels than non-ventilated patients (p=0.004 and p<0.001, respectively). The area under thereceiver-operating characteristic curve of RDW levels for predictingmechanical ventilation requirement was 0.716 (95% CI: 0.581-0.852, p=0.010). RDW had a sensitivity of 73%, specificity of 70%, and negative predictive value of91% with a cut-off value of 14.5% in predicting mechanical ventilation requirement in patients with organophosphate poisoning

Shaikh Mohammed Aslam et al studied A total of 158 patients of OPI were studied retrospectively from January 2005 to December2014. The diagnosis of a case of OPI poisoning was based on a clinical history of intentional ingestion of OPI and presence of characteristic signs and symptoms of OPI poisoning, and laboratory evidence of decreased serum cholinesterase activity. They observed that

Mean age was 31.32 ± 11.84 years and 58.2% of the patients were males. Mean serum pseudocholinesterase level was 5.5± 4.3 and mean RDW was 13.07± 1.67. Mortality rate was 8.9%. Non survivors had higher RDW (13.87± 2.81) when compared with survivors (12.99± 1.49). RDW had a sensitivity of 57.1%, specificity of 68.1%, and negative predictive value of 94.3% with a cut-off value of 13.5% in predicting mortality in patients with OPI poisoning.

Changwoo Kang et al conducted a retrospective analysis between January 2008 and July 2013 in patients admittedto the emergency department after OPI poisoning. A Kaplan-Meier 30-day survival curve was analyzed inpatients stratified according to the optimal cut-off point of RDW defined using a receiver operatingcharacteristic (ROC) curve. Multivariate Cox proportional hazards analyses were

conducted to determine the independent prognostic factors for 30-day mortality.

Results: Among 102 patients, 21 died, yielding a mortality of 20.6%. Elevated RDW was significantly associatedwith early mortality in patients with OPI poisoning. Levels of RDW that exceeded 13.5% (hazard ratio, 2.64;95% confidence interval [CI], 1.05-6.60) were associated with increased mortality in the multivariate analysis.The area under the ROC curve of RDW was 0.675 (95% CI, 0.522-0.829)

MATERIALS AND METHODS

STUDY POPULATION:

SOURCE OF DATA:

The study will be conducted on 200 patients admitted to Government Rajaji Hospital & Madurai Medical College with history of organophosphate poisoning during the study period

Inclusion Criteria

- Clinical history of ingestion of OPI poison between age 13- 60 yrs

Exclusion Criteria

- Coningestion with other poison
- Prehospital cardiac arrest
- Transfer to another hospital
- Discharge against medical advise
- Coronary artery disease

- Hypertension
- Diabetes
- Abnormal liver function test
- Abnormal renal function test
- Iron deficiency anaemia

DATA COLLECTION:

Informed consent will be obtained from all patients/attenders to be enrolled for the study. In all the patients relevant information will be collected in a predesigned proforma. The patients are selected based on clinical examinations and biochemical tests.

LABORATORY INVESTIGATIONS

a) Complete Hemogram

b) Peripheral blood smear

c) Liver function test

d) Renal function test

e) Random blood sugar

f) PseudoCholinesterase level

Adult patients aged more than 12 years of age attending the casualty of Department of Medicine of Government Rajaji Hospital, Madurai with history of OPC poisoning were admitted. Complete hemogram, blood sugar, urea, creatinine and liver function tests, serum pseudocholinesterase etc were done. Patients with abnormal blood sugar values, elevated renal function tests and elevated liver function tests were excluded.

DESIGN OF STUDY:

Prospective study

PERIOD OF STUDY:

6 MONTHS

COLLABORATING DEPARTMENTS:

DEPARTMENT OF PATHOLOGY

DEPARTMENT OF BIOCHEMISTRY

ETHICAL CLEARANCE: Applied for

CONSENT: Individual written and informed consent.

ANALYSIS: Statistical analysis will be performed using appropriate tests as required according to data.

CONFLICT OF INTEREST: NIL

FINANCIAL SUPPORT: SELF

PARTICIPANTS:

200 patients between age 13 and 60 years who will be admitted in emergency department with history of Organophosphate poisoning with normal blood sugar , LFT and RFT, with no significant past medical illnesss, during the study period

DATA ANALYSIS:

The collected data will be entered in Microsoft Excel spreadsheet andanalyzed using Statistical Package for Social Sciences (SPSS) version17. The analysis of data was carried out by entering the codedinformation and generating tables. The data will be presented usingdescriptive statistics in form of tables and graphs. Results areexpressed as proportions with 95% confidence interval. Univariateanalysis was carried out using non –parametric Mann Whitney Test

tocompare the RDW and various parameters between two groups. Student T test was used. The ROC curve (Receiver operating curve) was used to determine the optimal cut off point for RDW for predicting mortality.

A total of 200 patients who consumed Organophosphate poison fulfilling the inclusion criteria were taken for this study.

RESULTS AND INTERPRETATION

The mean age group participated was 36.63yrs with RDW lesser than 46 having Standard deviation of 13.141 and 37.11 with RDW higher than 46 having Standard deviation of 12.78 as shown in Table 1

Table 1. Mean of Age in RDW higher & lesser than 46

RDW	<=46		>46		Total	
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation
Age	36.63	13.141	37.11	12.78	36.9	12.9

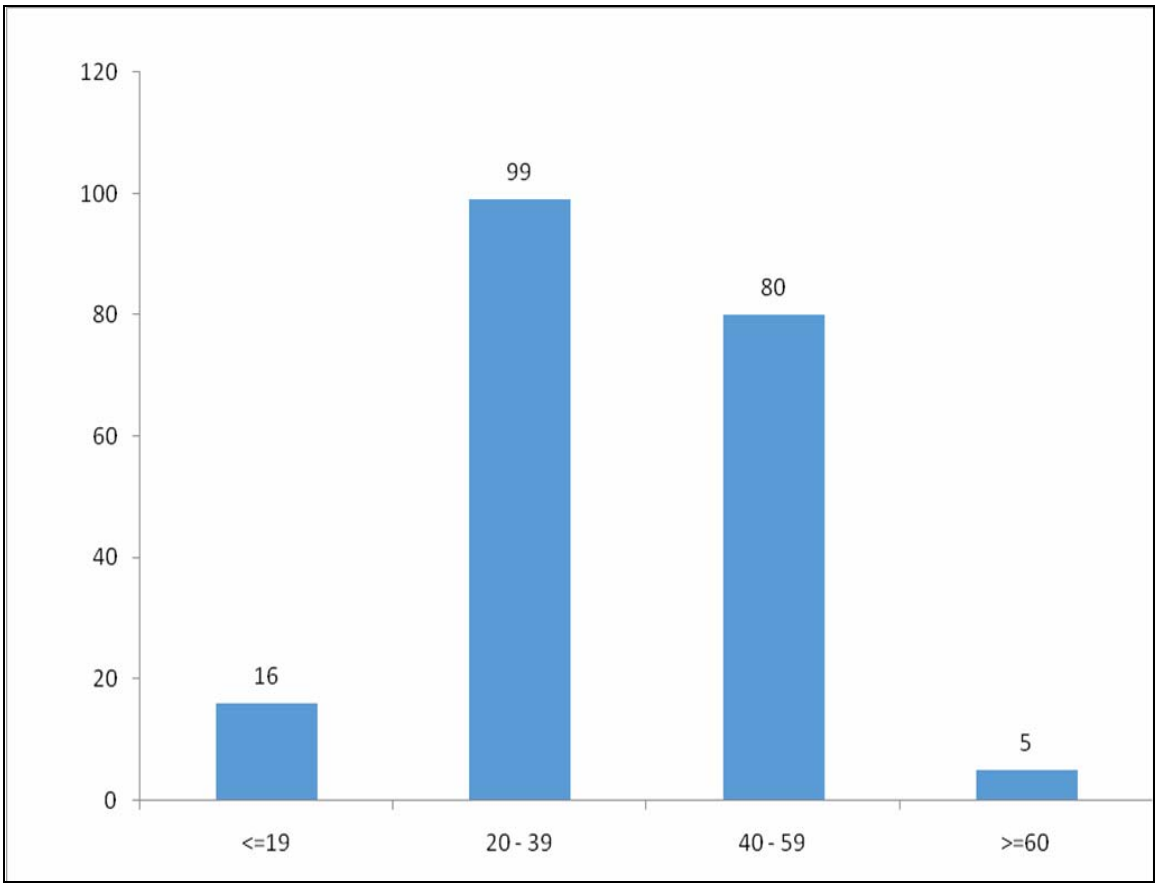
The age distribution was as shown in the table 2. Below 19 yrs there were 16 subjects(8%). Inbetween 20-39 yrs there were 99 subjects(49.5%) and 40-59 there were 80

subjects(40%). In the 60-70 yrs age group there were 5 subjects(2.5%). They were plotted and the bar diagram is as in figure1.

Table 2. Comparison of Age in RDW higher and lesser than 46

Age Group	Number	Percent
<=19	16	8.0
20 - 39	99	49.5
40 - 59	80	40.0
>=60	5	2.5
Total	200	100.0

Figure 1. Age Distribution

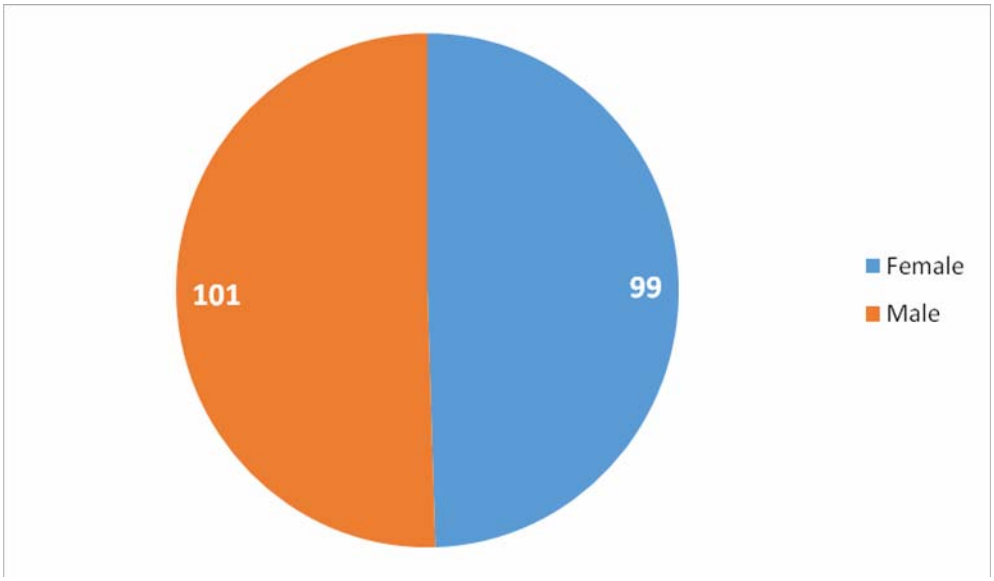


Out of 200 subjects number of males were 101(50.5%) and the number of females were 99 (49.5%) as shown in table 3. The sex wise distribution is shown in Figure 2

Table 3. Comparison of Sex in RDW higher and lesser than 46

Sex	Number	Percent
Female	99	49.5
Male	101	50.5
Total	200	100.0

Figure 2. Sex distribution

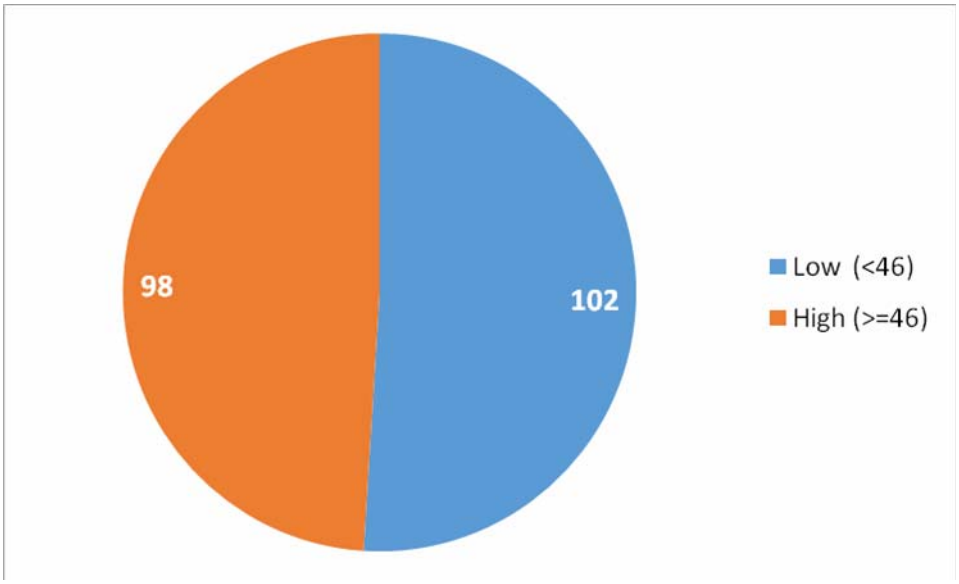


Among 200 subjects, the number of patients with RDW greater than or equal to 46 was 98(49%) and the number of patients with RDW lesser than 46 was 102(51%) as shown in table 4 and their distribution is shown in figure 3

Table 4. Comparison between RDW higher and lesser than 46

RDW	Number	Percent
Low (<46)	102	51.0
High (>=46)	98	49.0
Total	200	100.0

Figure 3. RDW Distribution



The mean value of RDW in less than 46 group was 39.64 with a standard deviation of 2.609 and in the RDW greater than 46 group was 50.72 with a standard deviation of 3.236 as shown in table 5. The mean of RDW of all 200 subjects was 45.1 with a standard Deviation of 6.3

Table 5. Mean of RDW value measured

RDW	<=46		>46		Total	
	Mean	Std. Deviation	Mean	Std. Deviation	Mean	Std. Deviation
RDW	39.64	2.609	50.72	3.236	45.1	6.3

Each subjects vitals blood pressure, SpO2, pulse rate, respiratory rate were measured on day 1 and day 3. Serum Pseudocholinesterase was also measured on day 1 and Day 3 of ingestion of Organophosphate poisoning

The mean of Systolic Bp, Diastolic Bp, Pulse rate , Respiratory rate, SpO2 and Serum Pseudocholinesterase were measured and shown in Table 6. Mean of SBP was 109.7 on Day 1 and 108.2 on Day 3. Mean of DBP was 72.9 on Day 1 and 79.5 on Day 3. The mean Pulse rate was 91.4

on Day 1 and 80.9 on Day 3 and respiratory rate was 19.1 on Day 1 and 15 on Day 3. The SpO2 was 84.3 on Day 1 and 91.5 on Day 3.

The mean Serum Pseudocholinesterase was 4200.8 on day 1 and 5987.4 on day 3

Table 6. Mean of Vitals and Serum Pseudocholinesterase

RDW	**Day 1**		**Day 3**	
	Mean	Std. Deviation	Mean	Std. Deviation
SBP	109.7	30.4	108.2	15.6
DBP	72.9	10.5	79.5	12.1
PULSE RATE	91.4	16.5	80.9	20.1
RESPIRATORY RATE	19.1	5.9	15.0	3.5
SpO2	84.3	11.6	91.5	4.2
Serum Pseudocholinesterase	4200.8	2947.1	5987.4	1208.3

The mean distribution of vitals were plotted and shown as follows in Figures 4 to 9

Figure 4. Distribution of SBP

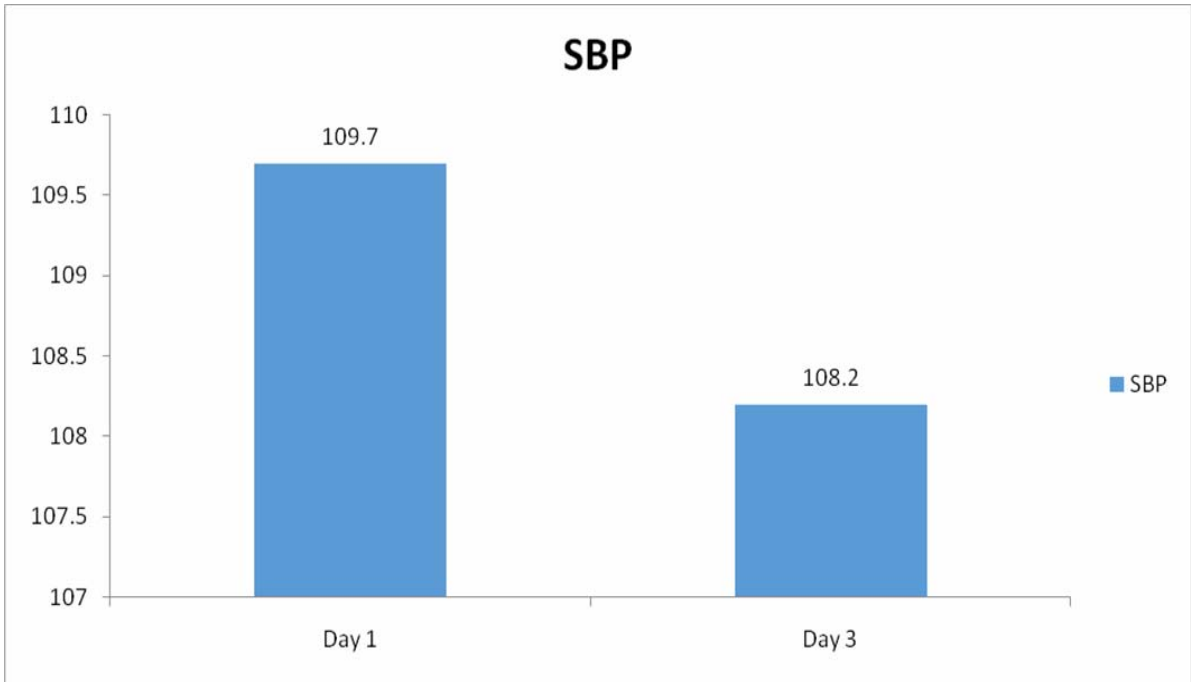


Figure 5. Distribution of DBP

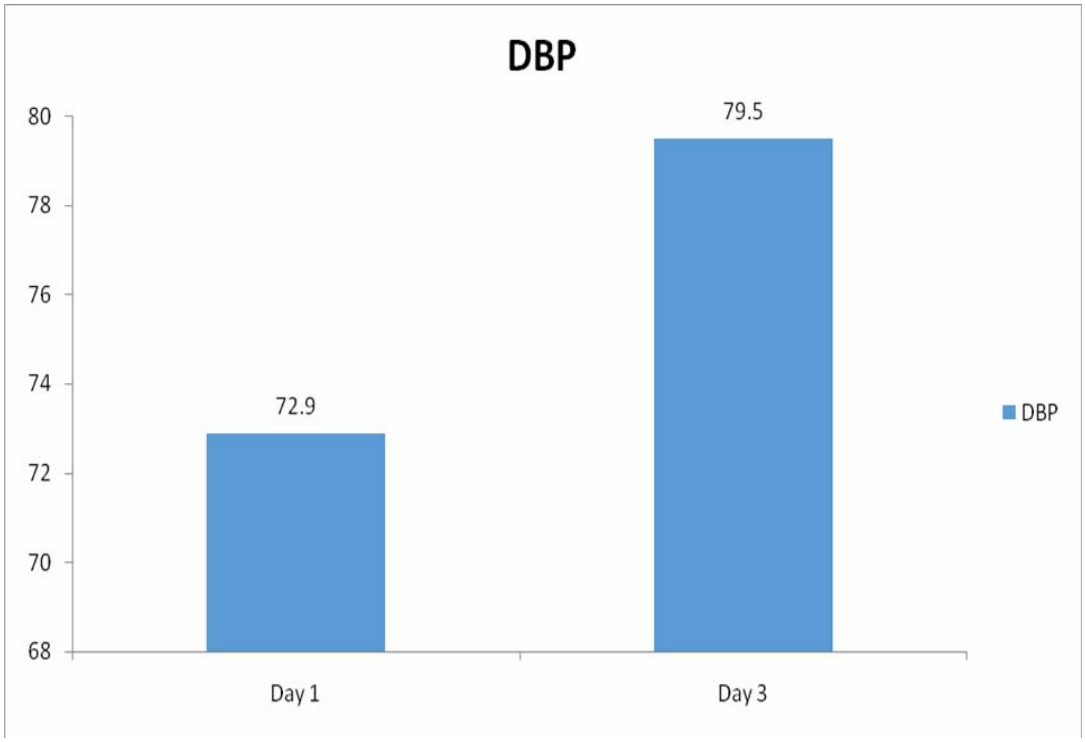


Figure 6. Distribution of Pulse Rate

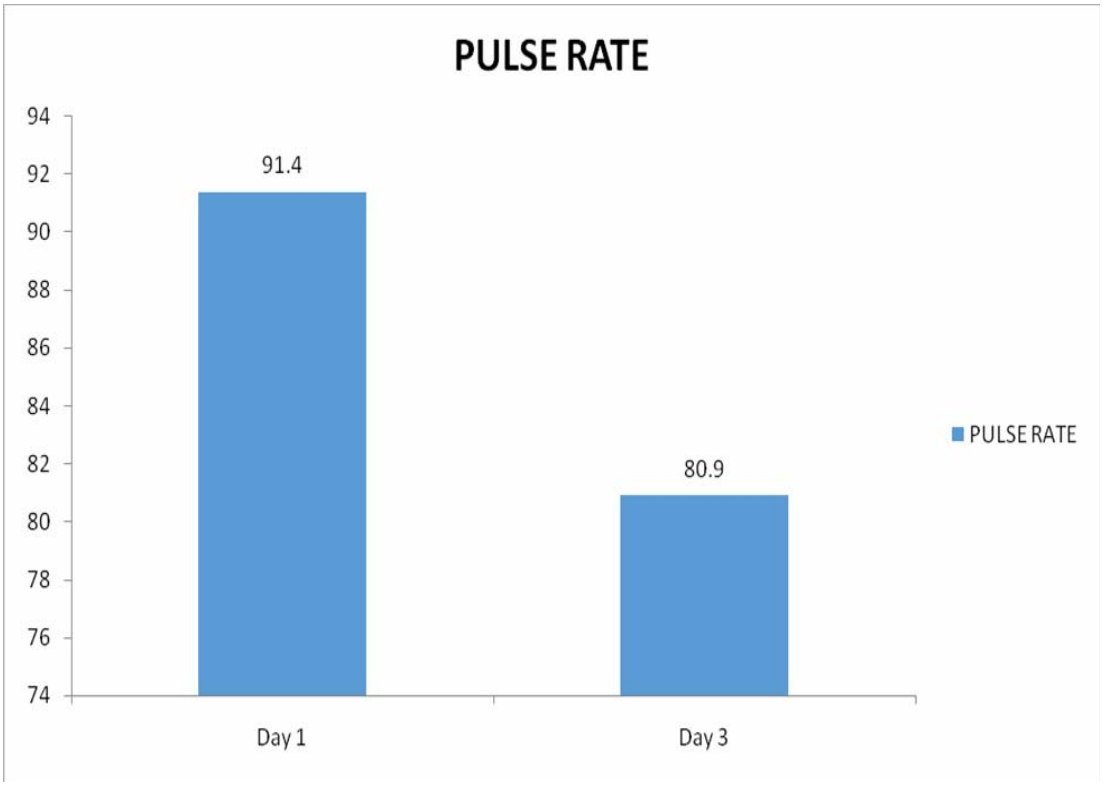


Figure 7. Distribution of SpO2

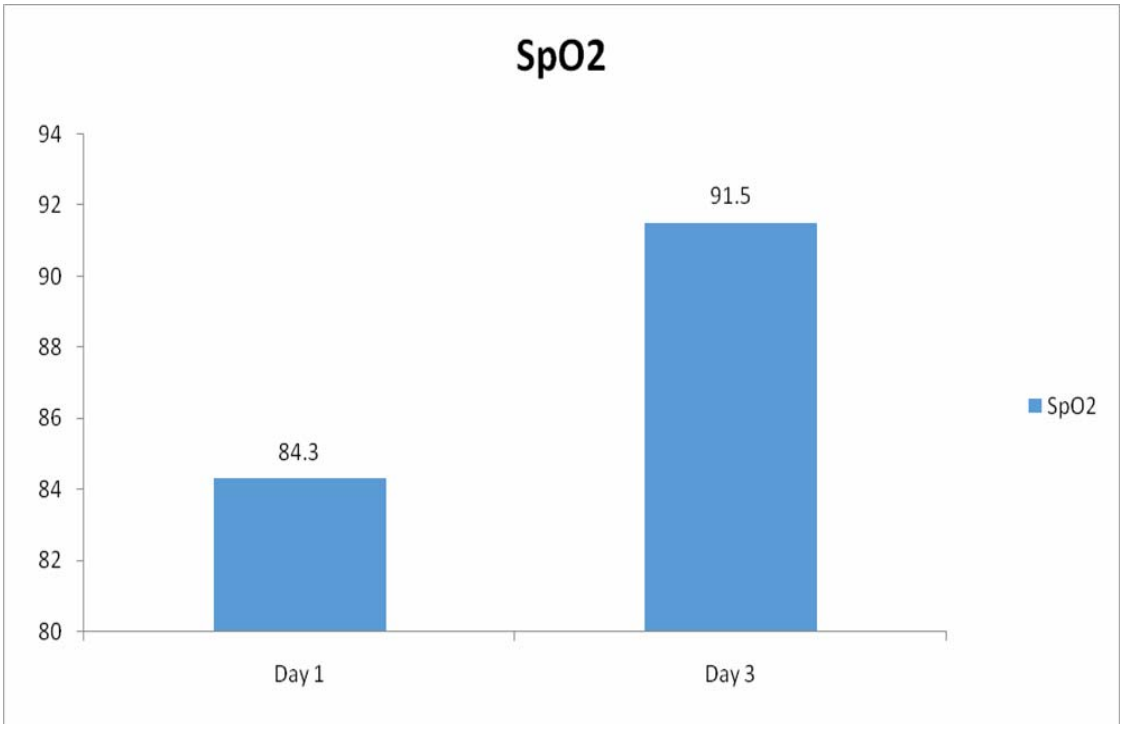


Figure 8. Distribution of Respiratory Rate

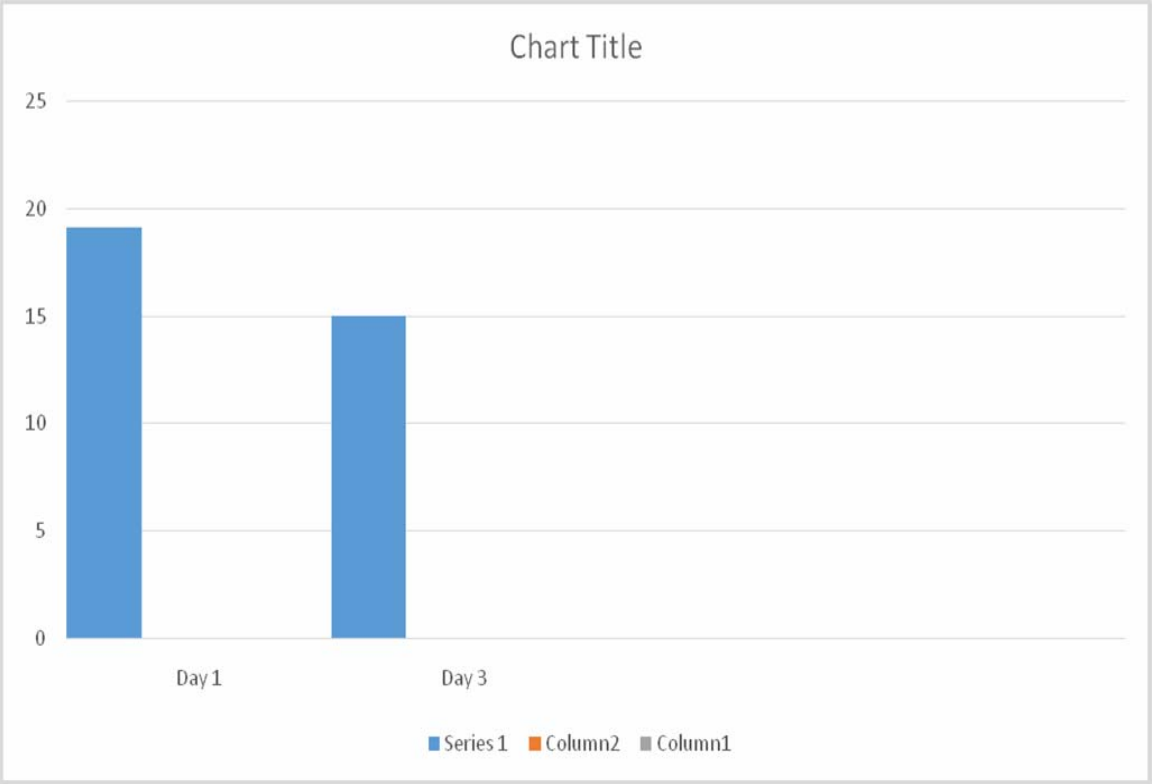
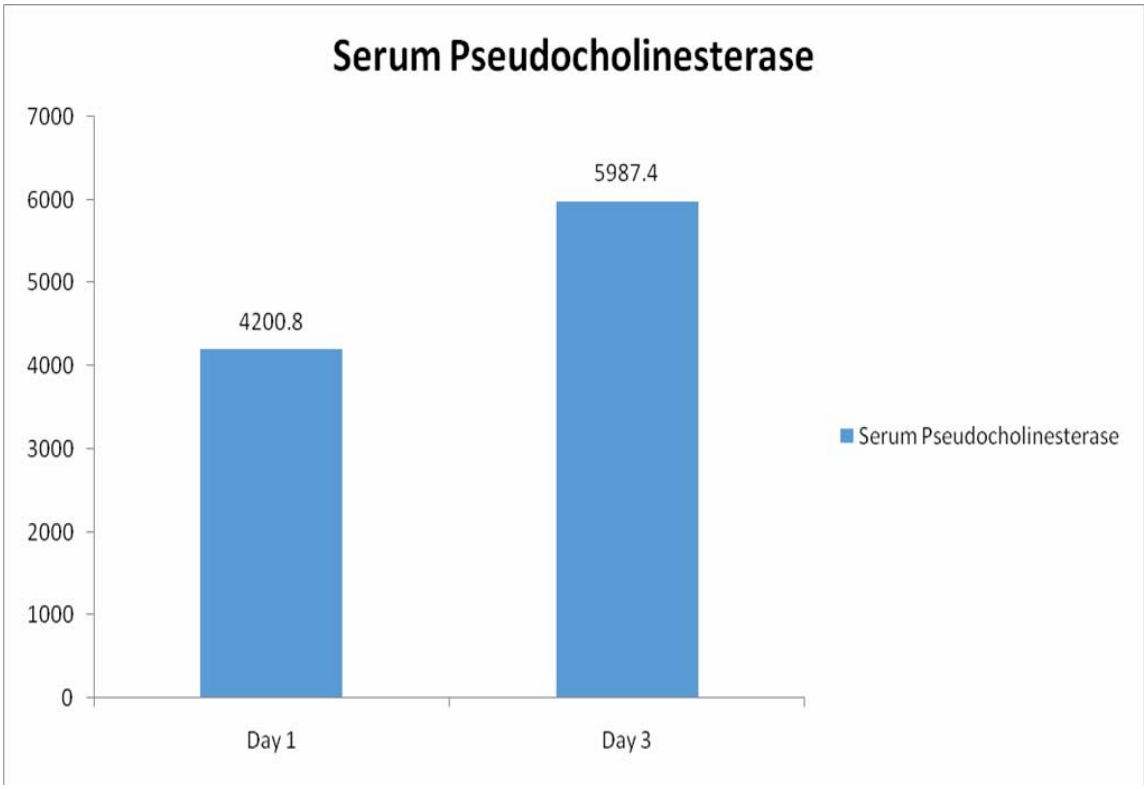


Figure 9. Serum Pseudocholinesterase Distribution



The same parameters were varied with RDW higher and lesser than 46 groups. The mean SBP on Day 1 was 107.43 and 112.06 in RDW low and higher than 46 respectively and on Day 3 was 118.27 and 97.61 in RDW low and High groups.

The mean DBP on Day 1 and Day 3 were 75.2 and 80.09 in RDW lesser than 46 . In RDW greater than 46 it was 70.45 and 78.8 on Day 1 and Day 3 respectively

The mean Pulse rate on Day 1 and Day 3 were 91.06 and 68.24 in RDW lesser than 46 . In RDW greater than 46 it was 91. and 68.54 on Day 1 and Day 3 respectively

The mean Respiratory Rate on Day 1 and Day 3 were 20.01 and 16.21 in RDW lesser than 46 . In RDW greater than 46 it was 18.2 and 13.66 on Day 1 and Day 3 respectively

The mean SpO2 on Day 1 and Day 3 were 92.72 and 91.22 in RDW lesser than 46 . In RDW greater than 46 it was 75.53 and 91.84 on Day 1 and Day 3 respectively

The mean Pseudocholinesterase on Day 1 and Day 3 were 6603.56 and 6107.12 in RDW lesser than 46 . In RDW greater than 46 it was 1699.89 and 5862.84 on Day 1 and Day 3 respectively

Table 7. Comparison of mean of Parameters on Day 1 and 3

RDW	Day 1			Day 3		
	Low	High	Total	Low	High	Total
Parameters	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
SBP	107.43 (30.6)	112.06 (30.1)	109.7 (30.4)	118.27 (12.3)	97.61 (11.0)	108.2 (15.6)
DBP	75.2 (9.1)	70.45 (11.2)	72.9 (10.5)	80.09 (11.9)	78.8 (12.2)	79.5 (12.1)
Pulse Rate	91.06 (16.7)	91.7 (16.3)	91.4 (16.6)	92.75 (16.8)	68.54 (15.2)	80.9 (20.1)
Respiratory Rate	20.01 (5.9)	18.2 (5.6)	19.1 (5.9)	16.21 (3.7)	13.66 (2.6)	15.0 (3.5)
SpO2	92.72 (6.6)	75.53 (8.7)	84.3 (11.6)	91.22 (4.3)	91.84 (3.9)	91.5 (4.2)
Serum Pseudocholinesterase	6603.56 (1841.4)	1699.89 (1377.6)	4200.8 (2947.1)	6107.12 (1232.7)	5862.84 (1175.8)	5987.4 (1208.3)

The distribution of the parameters were inputted and compared between day 1 and day 3 of RDW higher than 46 and Lesser than 46 groups and shown in Figures 10 – 15

Figure 10. Distribution of SBP

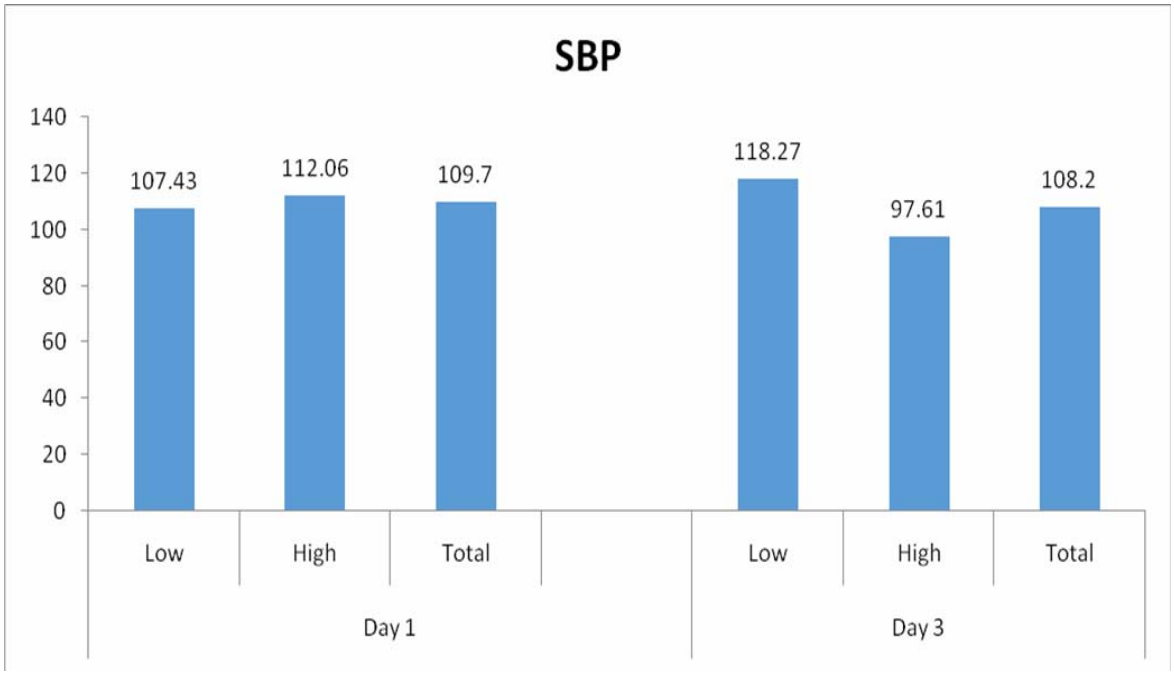


Figure 11. Distribution of DBP

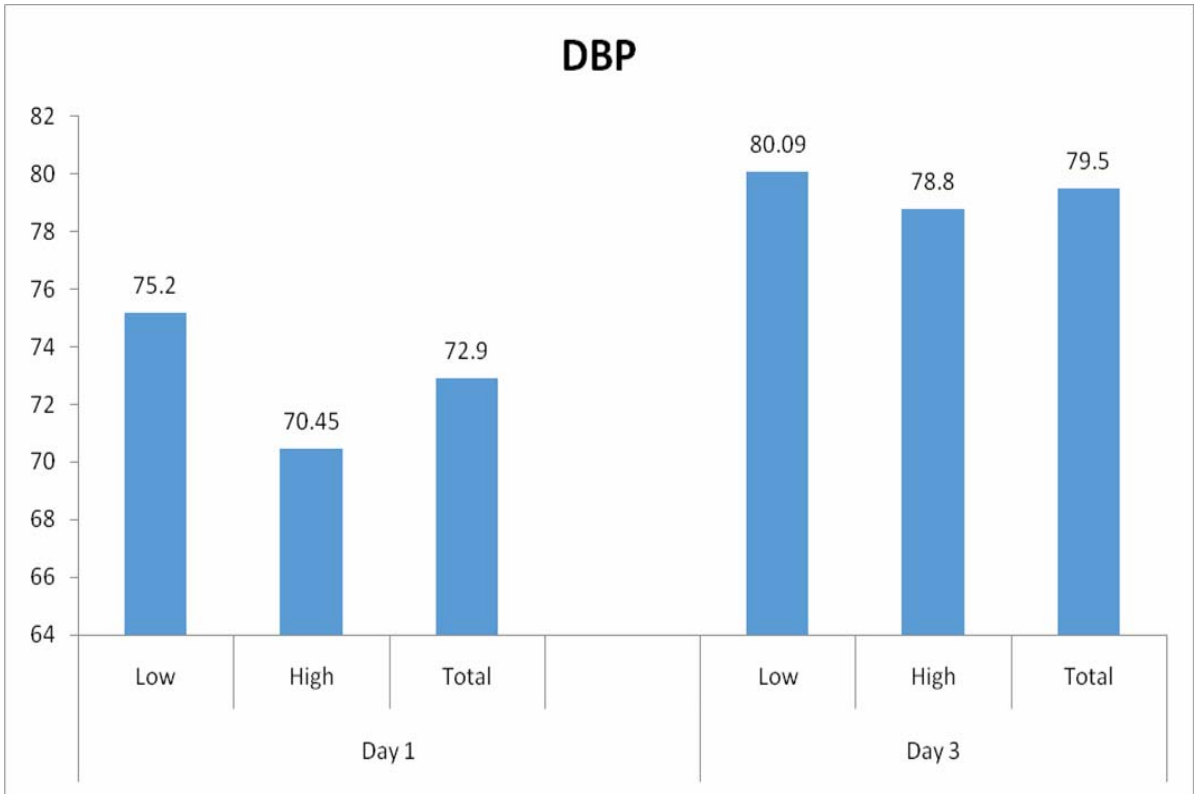


Figure 12. Distribution of Pulse Rate

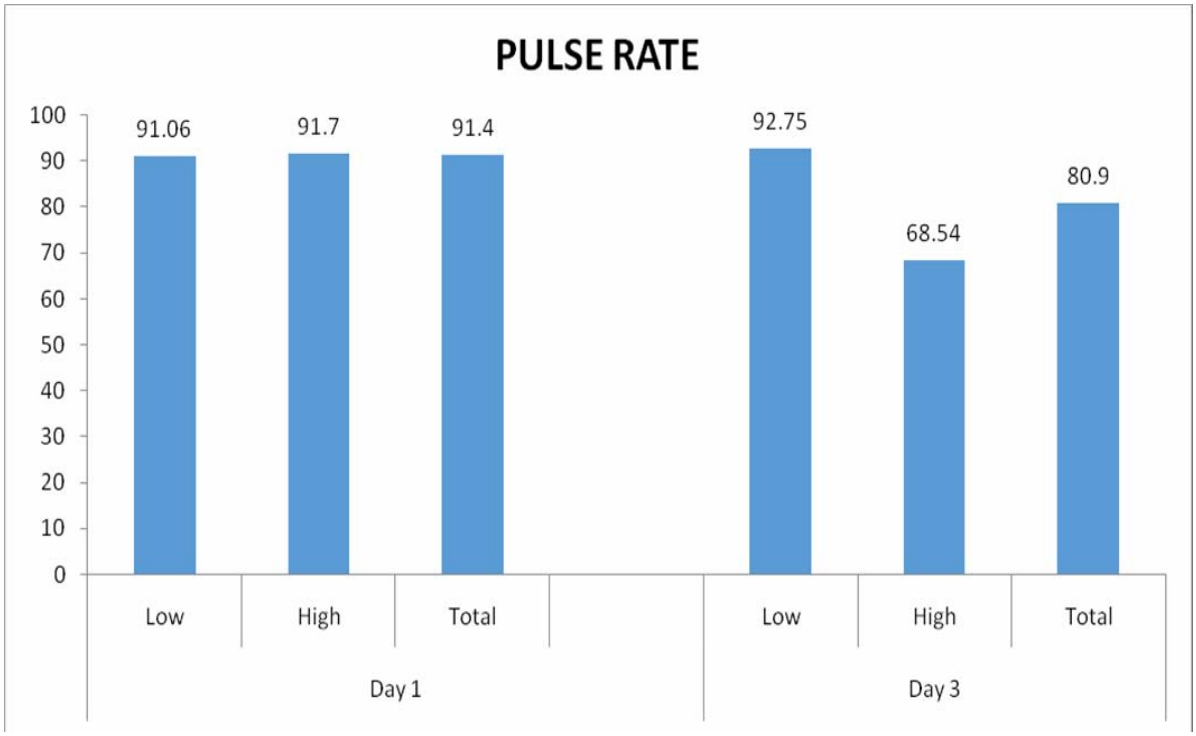


Figure 13. Distribution of Respiratory Rate

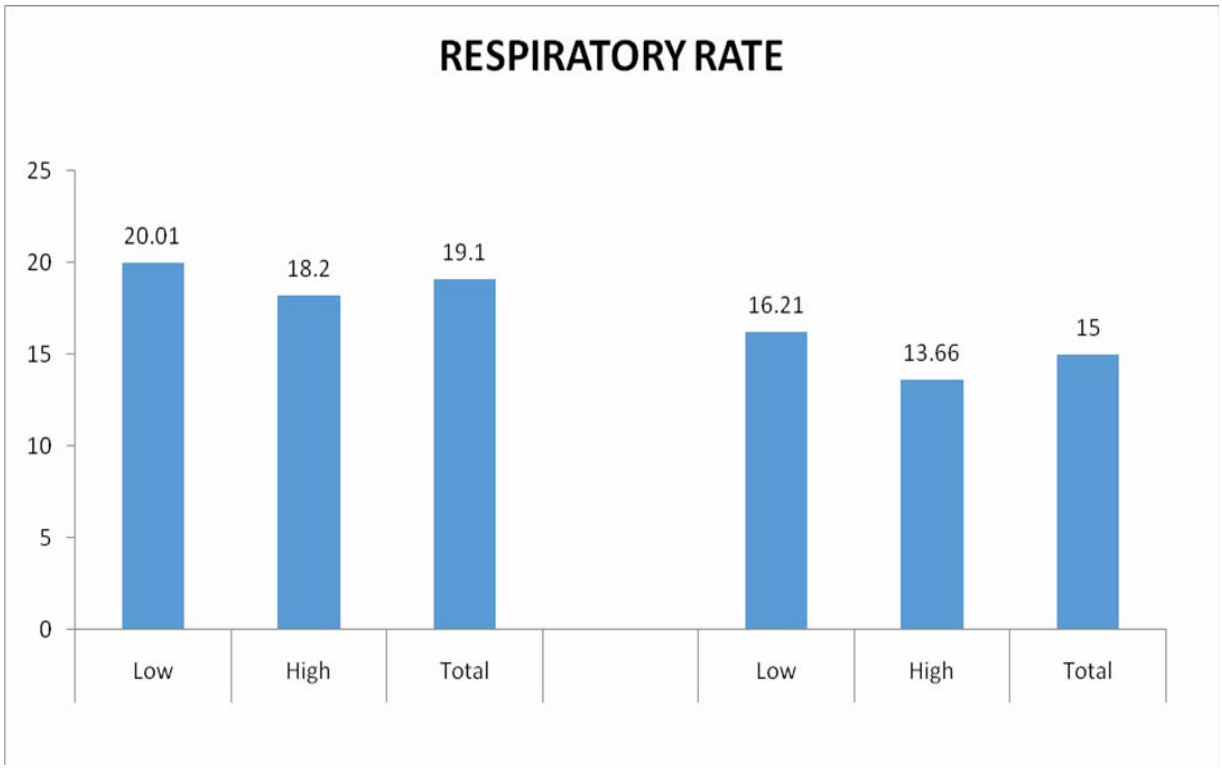


Figure 14. Distribution of SpO2

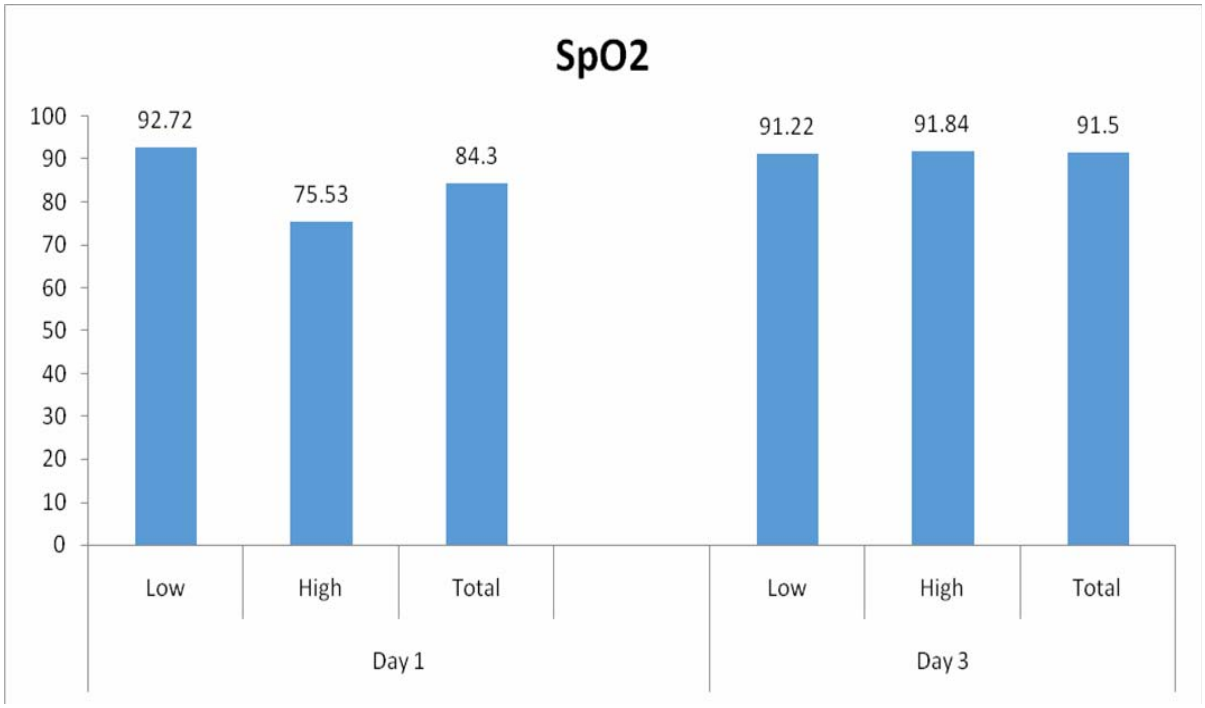
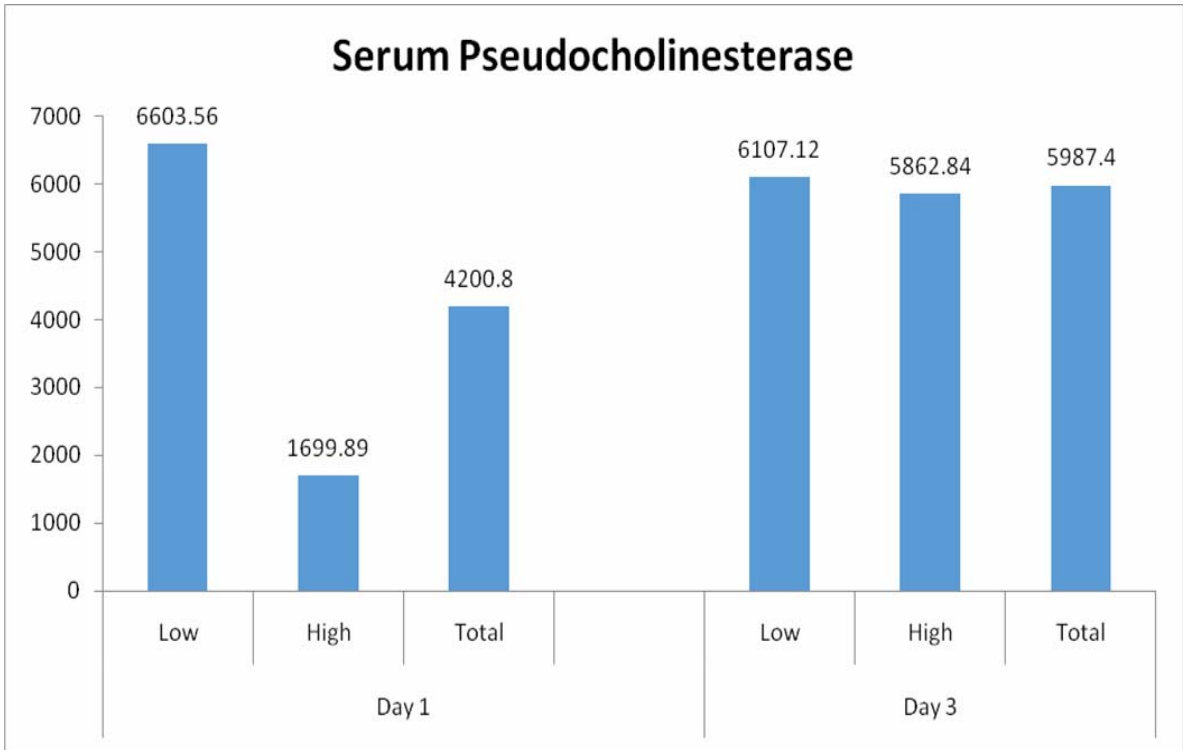


Figure 15. Distribution of Serum PseudoCholinesterase



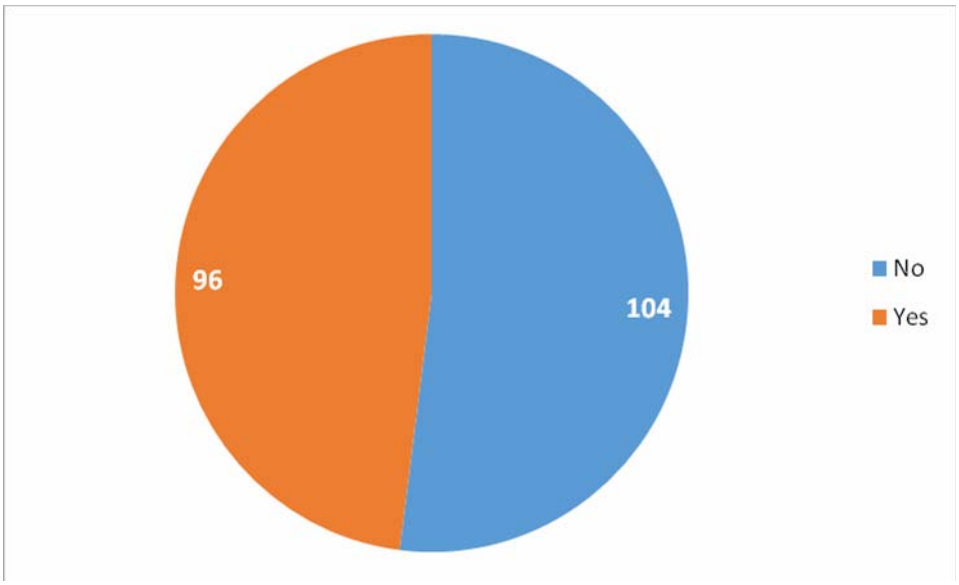
The outcomes were measured as no adverse effects, early intubation, those needing tracheostomy and death within 30 days and tabulated as follows

Out of 200 subjects those with no adverse effects were 104 (52%) and with adverse effects were 96(48%) as shown in table 8 and and the distribution is shown in figure 16

Table 8. Comparison of Adverse effects

No Adverse Effects	Number	Percent
No	104	52.0
Yes	96	48.0
Total	200	100.0

Figure 16. Distribution of Adverse effects group

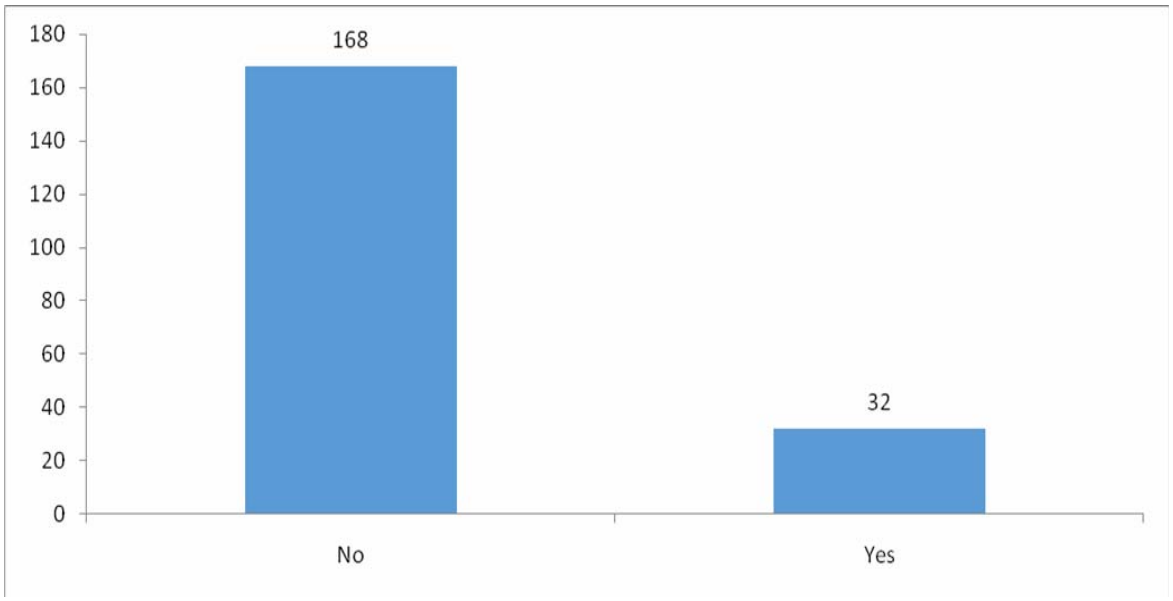


Among those with adverse effects, 32(16%) were intubated and extubated within 5 days as shown in table 9 and its distribution as in figure 17

Table 9. Comparison of Intubated and Early Extubated

Intubated and early extubated	Number	Percent
No	168	84.0
Yes	32	16.0
Total	200	100.0

Figure 17. Distribution of Intubated and Early Extubated

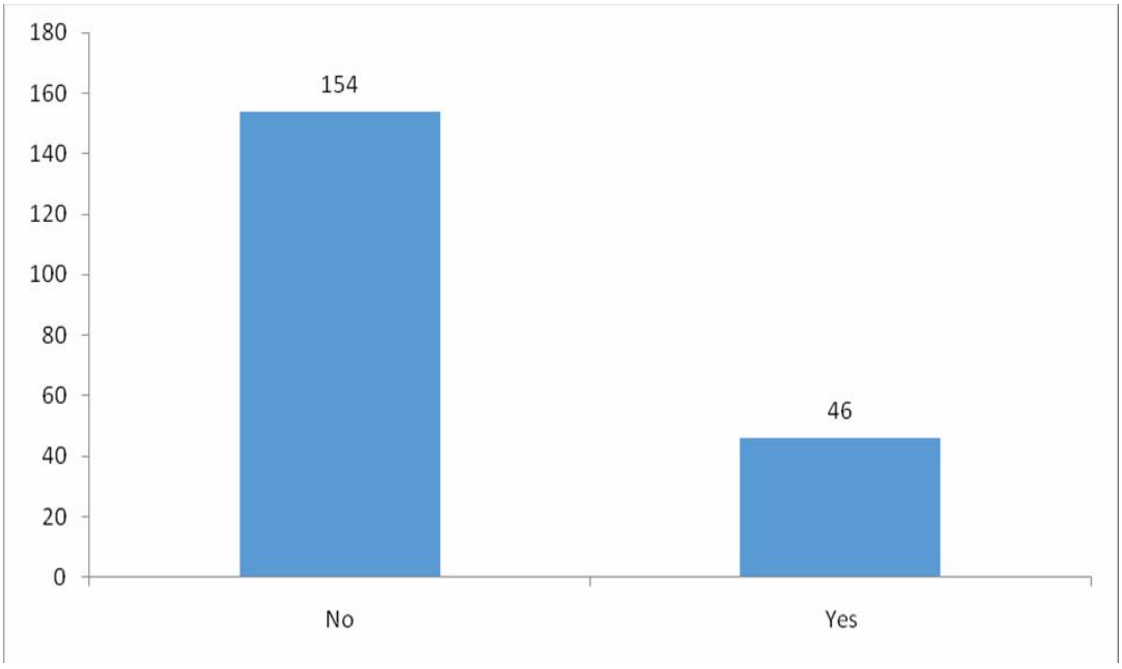


Among those 200, 46(23%) were intubated and needing prolonged duration of ventilation more than 5 days and underwent tracheostomy shown in table10 and the distribution in figure 18

Table 10. Comparison of intubated and Needing Tracheostomy

Intubated needing tracheostomy	Number	Percent
No	154	77.0
Yes	46	23.0
Total	200	100.0

Figure 18. Distribution of intubated and Needing Tracheostomy

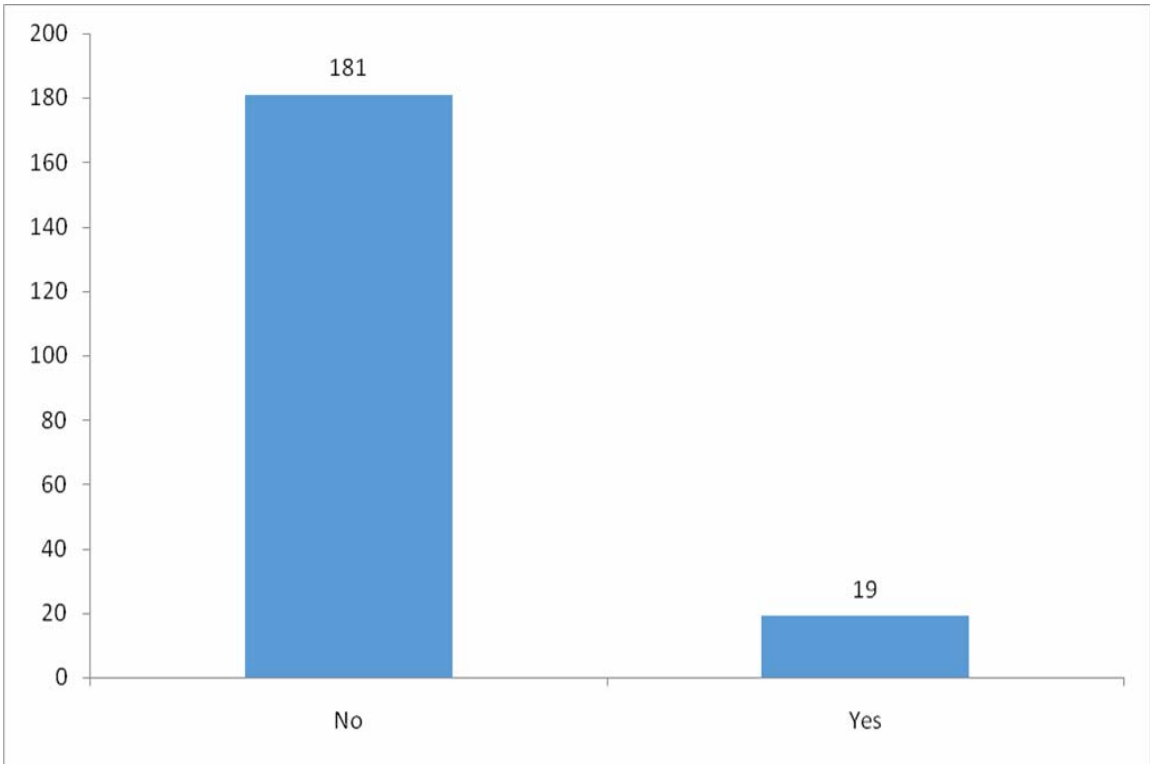


Of the 200, 19(9.5%) had delayed respiratory failure needing mechanical ventilation as shown in table 11 and the distribution is shown in figure 18

Table 11.Comparison of Delayed Respiratory failure within 72 hrs

Delayed respiratory failure within 72hrs	Number	Percent
No	181	90.5
Yes	19	9.5
Total	200	100.0

Figure 19. Distribution of Delayed Respiratory failure within 72 hrs

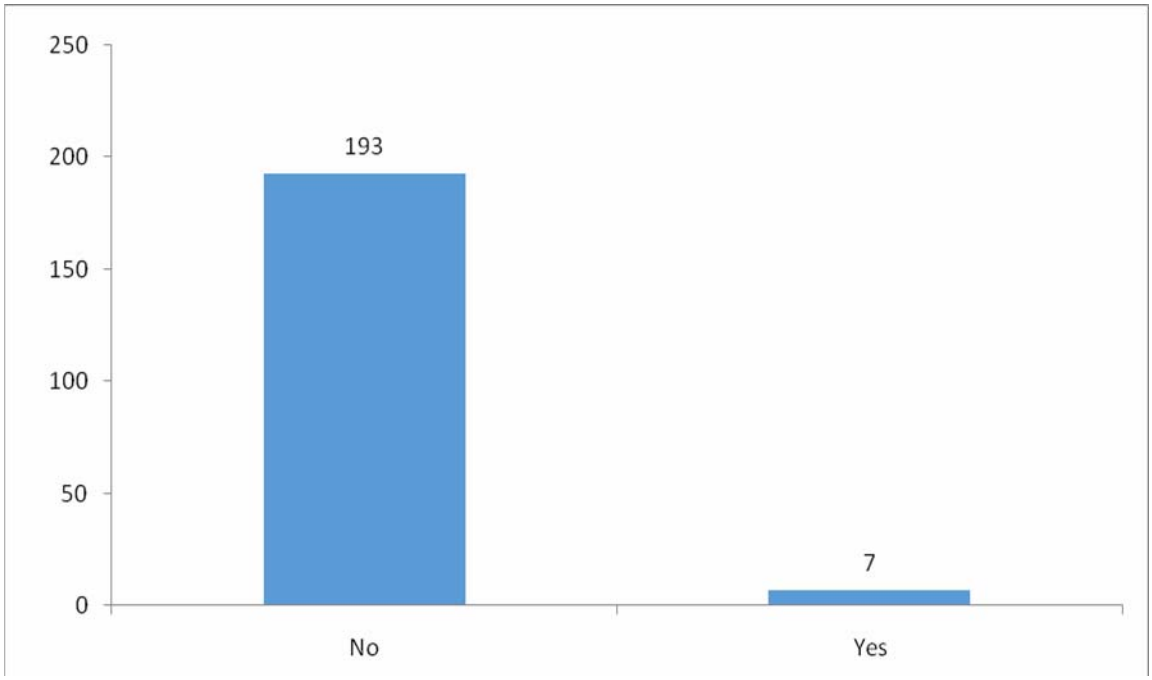


There were 7 deaths (3.5%) in the study population as shown in table 12 and their distribution is depicted figure 20

Table 12. Comparison of Death within 30 days

Death within 30 days	Number	Percent
No	193	96.5
Yes	7	3.5
Total	200	100.0

Figure 20. Distribution of Death within 30 days



In the RDW higher group there were 7 patients with no adverse effects, 19 who were intubated and extubated early. 46 subjects were intubated and needed prolonged mechanical ventilation beyond 5 days and hence underwent elective tracheostomy. 19 had delayed respiratory failure within 72 hrs requiring mechanical ventilation and 7 died within 30 days in the RDW higher than 46 group. The comparison is shown in table 13

Table 13. Comparision of Outcomes

Outcomes	RDW Low			RDW High		
	No	Yes	Total	No	Yes	Total
No adverse effects	13	89	102	91	7	98
Intubated and early extubated	89	13	102	79	19	98
Intubated needing tracheostomy	102	0	102	52	46	98
Delayed respiratory failure within 72hrs	102	0	102	79	19	98
Death within 30 days	102	0	102	91	7	98

Comparison between the baseline parameters and RDW using Student t-test:

The P-value <0.05 is taken as statistically significant

Table 14. Comparison of baseline parameters and RDW

RDW	Low		High		P-value
	Mean	Std. Deviation	Mean	Std. Deviation	
Age	36.6	13.1	37.1	12.8	0.792
SBP	107.4	30.7	112.1	30.2	0.283
DBP	75.2	9.2	70.4	11.2	0.001
PULSE RATE	91.1	16.7	91.7	16.3	0.783
RESPIRATORY RATE	20.0	6.0	18.2	5.7	0.030
SpO2	92.7	6.6	75.5	8.8	<0.0001
Serum Pseudocholinesterase	6603.6	1841.5	1699.9	1377.6	<0.0001

From the t test we derive that the mean serum pseudocholinesterase was lower in RDW high group 1699(SD 1377.6) than the RDW low group 6603.6(SD1841.5) which is statistically significant ($p<0.0001$)

Also the mean SpO2 was lower in the RDW higher group 75.5 (SD 8.8) and higher in RDW 92.7 (SD 6.6) which is also statistically significant ($p<0.0001$)

Also the mean Respiratory Rate was lower in the RDW higher group 18.2 (SD 5.7) and higher in RDW 20 (SD 6.0) which is also statistically significant ($p<0.030$)

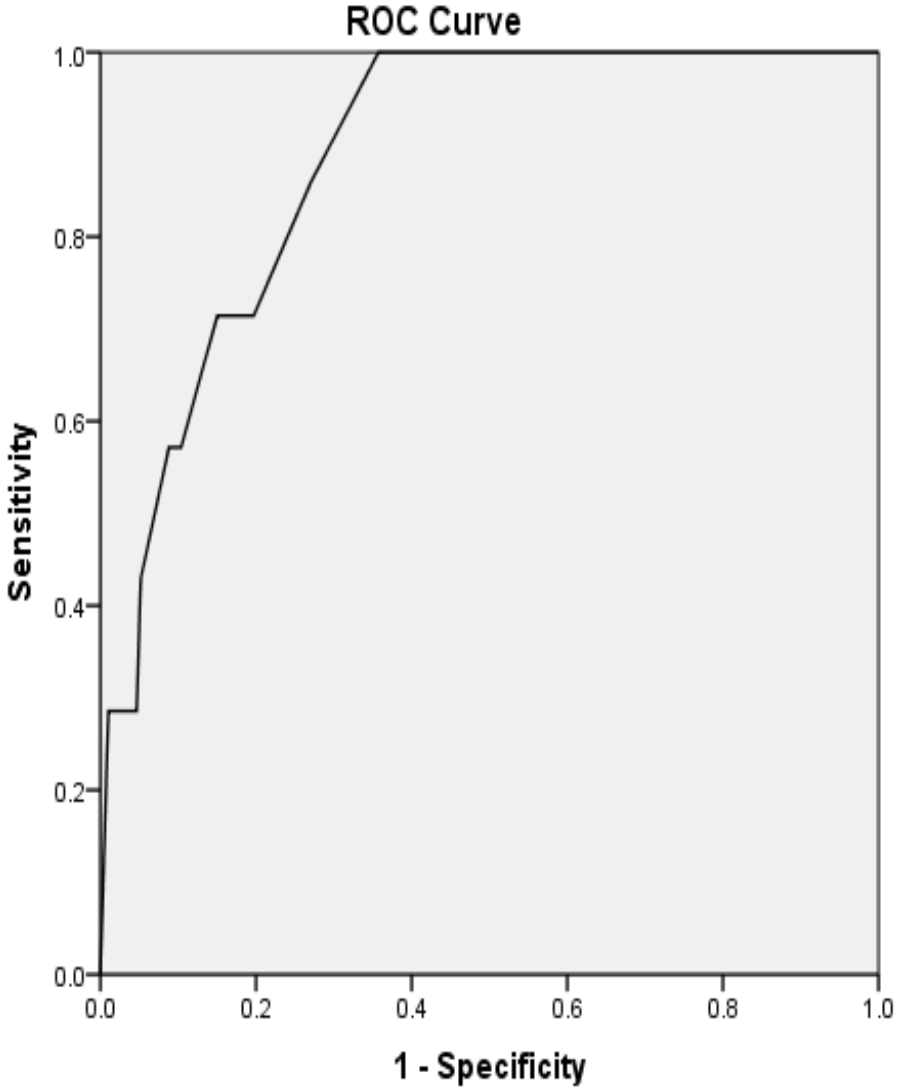
Also the mean Diastolic BP was lower in the RDW higher group 70.4 (SD 11.2) and higher in RDW 75.2 (SD 9.2) which is also statistically significant ($p<0.001$)

The other parameters like age, Systolic Bp Pulse Rate did not have statistical significance.

Patients with RDW high than 46 had very low Serum Pseudocholinesterase, Lower SpO2, Diastolic BP and Respiratory Rate which were statistically significant.

ROC (Receiver operating curve) was used to determine the optimal cut off point for RDW for predicting mortality.

RDW had a sensitivity of 71.4 % and the specificity of 85 % with a cut-off value of 51.5 in predicting mortality in patients with OPI poisoning.



Area Under the Curve: 0.885

DISCUSSION

DISCUSSION:

Organophosphate poisoning causes many hematological and biochemical changes on accidental or toxic exposure. It causes increased inflammatory cytokines particularly IL-1b, IL-8 that causes oxidative stress damaging the RBC membranes leading to anisocytosis and elevated RDW. Organophosphate poisoning also reduces certain anti-inflammatory cytokines such as IL-10 further tipping the balance between pro and anti-inflammatory state in the body leading to oxidant damage.

The principle oxidant involved is SOD (superoxide dismutase) which damages the RBC membrane by lipid peroxidation of the phospholipid membrane layer releasing Malonylaldehyde. It also reduces the level of total

cholesterol and phospholipid in the RBC membrane making it unstable and prone to sheer stress and alter RBC’s shape

Also Organophosphates have redox cycling activity, i.e. they accept a free electron and transfer it to O2 causing free radical generation, thereby oxidant damage.

RBC’s are prone to damage easily as they have no nucleus and mitochondria. This makes them easily affected especially during hypoxia which is the feature of Organophosphate poisons.

Hypoxia damages the RBC membrane as it leads to auto-oxidation of Hemoglobin (Hb is degraded to methHb)thereby decreasing its oxygen carrying capacity and less affinity with shift of Hb-O2 dissociation curve to right.

This leads to RBC membrane damage and it continues as a vicious cycle until intervened.

The mean age group participated was 36.63yrs with RDW lesser than 46 having Standard deviation of 13.141 and 37.11 with RDW higher than 46 having Standard deviation of 12.78. Out of 200 subjects number of males were 101(50.5%)

In study by ***Shaikh Mohammed Aslam et al***, the mean age was 31.32 ± 11.84 years. 58.2% of the patients were males. Mean heart rate was 102.10± 21.33 beats per minute and mean respiratory rate was 22.34±16.13 cycles per minute.

Hence our study was correlating with the above study on basis of age and sex.

In our study, the mean Respiratory Rate on Day 1 was 20.01 in RDW lesser than 46 . In RDW greater than 46 it was 18.2 on Day 1

The mean SBP on Day 1 was 107.43 and 112.06 in RDW low and higher than 46 respectively and on Day 3 was 118.27 and 97.61 in RDW low and High groups.

In study by ***Changwoo Kang et al,*** the mean SBP (mm Hg) was 136.3 ± 37.7 with Total patients, 139.2 ± 36.5 with RDW lower groupand 127.5 ± 40.9 with RDW higher group.

The mean Respiratory rate(breaths per minute) was in total group 21.8 ± 11.6, RDW low group 21.0 ± 6.0 and in RDW high group 24.2 ± 21.0.

In our study there were 7 deaths among 200 patients (3.5%) with all of them having elevated RDW levels. None died in the RDW lower group

In study by ***Zerrin Define Dundar et al,***7 (9.7%) died during the intensive care unit follow-up period. The patients who died had higher median RDW levels than survivors[15.40 (15.10-16.40) and 14.30 (13.30-16.00), respectively, p=0.047]

SUMMARY

SUMMARY:

A total of 200 patients Government Rajaji Hospital, Madurai were recruited for thisobservational study.

In the RDW higher than 46 group there were 7 patients with no adverse effects, 19 who were intubated and extubated early.

46 subjects were intubated and needed prolonged mechanical ventilation beyond 5 days and hence underwent elective tracheostomy.

19 had delayed respiratory failure within 72 hrs requiring mechanical ventilation and 7 died within 30 days in the RDW higher than 46 group.

In the RDW lesser than 46 group there were 89 patients with no adverse effects, 13 who were intubated and extubated early.

Zero subjects were intubated and needed prolonged mechanical ventilation beyond 5 days

None had delayed respiratory failure within 72 hrs requiring mechanical ventilation and no one died within 30 days in the RDW lesser than 46 group.

The RDW high group had lower mean Serum Pseudocholinesterase 1699(SD 1377.6) which is statistically significant

Also RDW higher group had low SpO2 75.5 (SD 8.8), respiratory rate 18.2 (SD 5.7) and Diastolic BP 70.4 (SD 11.2) which is also statistically significant

RDW had a sensitivity of 71.4 % and the specificity of 85 % with a cut-off value of 51.5 in predicting mortality in patients with OPI poisoning.

LIMITATION:

- Our study did not involve any intervention.
- The subtype of Organophosphate poison a nd their outcomes were not studied separately.
- We did not include other types of poison like Carbamate, organochlorines
- We could not quantify the amount of exposure that occurred in each patient
- The height, weight, BMI of patients were not studied, since Organophosphate poisons are fat soluble
- The study had smaller group of population from a Single Institution which may not represent the whole Indian population

- The levels of folic acid, vitamin B12, and iron that might influence the RDW value were not measured

CONCLUSION:

Red cell distribution width is a quick, simple, easy and effective tool to risk stratify Organophosphate poisoning cases in low income, resource poor settings and in most situations where the degree of exposure to poison could not be assessed or wasn’t revealed

It can be used as an additional tool to predict complications in patients with Organophosphate poisoning and also as a criteria for discharging in-patients who are not at risk of intoxication.

Further studies involving larger group of populations representing various cultures and many subset of populations is needed

ANNEXURE

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PROFORMA

Name:

Age / Sex:

Occupation:

Presenting complaints:

Past History:

H/o DM, HT, CKD, CVD, DRUG INTAKE, Thyroid disorders, Alcohol intake

Clinical Examination:

General Examination:

Consciousness

Pallor

Jaundice

Clubbing

Lymphadenopathy

Hydration status

Signs suggestive of poisoning

Salivation

Lacrimation

Urination

Defeacation

Gastrc emesis

Bronchorrhea

Bronchospasm

Bradycardia

Vitals:

PR

Bp

RR

SpO2

Systemic examination:

CVS:

RS:

ABDOMEN:

CNS:

Laboratory investigations:

a) Hemoglobin

b) Hematocrit

c) Mean Corpuscular Volume

d) MCHC

e) Peripheral Smear

f) Liver function test

g) Renal function test

h) Red cell distribution width

ABBREVIATIONS

OPC/OPI – Organophosphate

Ache – Acetylcholinesterase

RDW – red cell distribution width

SpO2- Oxygen Saturation by Pulse oximetry

BP – Blood pressure

CONSENT FORM

ஆராய்ச்சி ஒப்புதல் படிவம்

பெயர்: தேதி:
வயது:
நோயாளிஎண்:
ஆராய்ச்சிசேர்க்கைஎண்:

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கங்களும் முழுமையாக எனக்கு விளக்கபட்டது.

எனக்கு விளக்கபட்ட விஷயங்களை நான் புரிந்துகொண்டு எனது முழுமனதுடன் சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில்தான் பங்கு பெறுகிறேன் மற்றும் நான் இந்த ஆராய்ச்சியில் இருந்து எந்த நேரமும் பின்வாங்கலாம் என்றும் அதனால் எந்த பாதிப்பும் எனக்கு ஏற்படாது என்பதையும் புரிந்து கொண்டேன்.

நான் என்னுடைய சுயநினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த மருத்துவ ஆராய்ச்சியில் பங்குகொள்ள சம்மதிக்கிறேன்.

MASTER CHART

Number	Age	Sex	SBPd1	SBPd3	DBPd1	DBPd3	PR d1	PR d3	RR d1	RR d3	SpO2d1	SpO2d3	PseudoChe D1	PseudoChe D3	RDW	No adverse effects	Intubated & early extubated	Intubated + tracheostomy	Delayed respiratory failure < 72hrs	Death< 30 days
1	35	M	122	83	54	96	60	74	21	14	83	97	594	6880	56	N	N	N	Y	N
2	23	M	62	113	80	83	118	105	13	19	95	85	7499	6669	36	Y	N	N	N	N
3	16	M	158	107	63	60	120	97	13	13	92	87	6959	6652	39	Y	N	N	N	N
4	55	F	100	121	67	94	60	68	28	11	90	86	7361	4897	42	Y	N	N	N	N
5	57	F	112	119	64	100	104	107	15	16	96	94	7730	5860	39	Y	N	N	N	N
6	32	F	76	118	90	73	117	97	11	18	98	89	6116	4503	39	Y	N	N	N	N
7	34	F	116	102	74	60	96	88	13	16	61	93	1832	7397	39	N	Y	N	N	N
8	45	F	160	140	72	71	63	85	11	19	83	97	1587	4449	36	N	Y	N	N	N
9	45	M	122	127	75	89	91	82	22	11	98	98	6189	6737	39	Y	N	N	N	N
10	42	F	66	133	88	81	119	99	25	11	91	90	6894	6041	39	Y	N	N	N	N
11	33	M	122	130	67	73	108	109	30	17	78	85	3364	5868	39	N	Y	N	N	N
12	55	M	66	124	84	63	78	83	23	22	95	88	8363	5382	34	Y	N	N	N	N
13	53	M	100	112	88	80	72	79	24	10	93	97	6605	4169	41	Y	N	N	N	N
14	32	F	118	137	76	83	111	99	26	14	73	89	3012	4989	36	N	Y	N	N	N
15	42	F	122	123	63	90	104	103	17	15	86	89	1878	5062	36	N	Y	N	N	N
16	46	F	60	105	81	89	66	76	10	24	92	98	5560	7073	36	Y	N	N	N	N
17	56	F	74	80	83	93	88	62	30	12	61	90	856	7102	49	N	Y	N	N	N
18	44	M	150	86	64	95	64	70	30	16	65	96	1252	7104	49	N	N	N	Y	N
19	33	F	138	85	52	88	77	57	30	18	80	91	1883	7837	47	N	Y	N	N	N
20	21	F	68	102	64	68	112	69	25	12	63	85	1351	5890	51	N	N	Y	N	N
21	22	M	62	89	81	81	75	79	30	12	87	85	1725	4610	52	N	N	Y	N	N
22	25	F	100	108	83	83	84	74	30	10	88	92	992	4700	59	N	N	N	N	Y
23	24	F	124	86	88	94	108	57	15	11	62	93	2000	4966	57	N	N	Y	N	N
24	36	M	66	93	58	93	111	54	17	15	70	98	1221	7127	56	N	Y	N	N	N
25	35	F	152	83	61	75	80	77	17	18	80	94	1995	5211	54	N	N	N	N	Y
26	31	M	98	80	57	91	74	71	14	17	61	98	716	7269	58	N	N	Y	N	N
27	23	F	156	90	52	62	98	57	24	10	61	90	1421	4860	50	N	N	Y	N	N
28	29	F	154	138	87	84	85	91	21	20	94	90	7665	6869	39	Y	N	N	N	N
29	38	F	66	131	83	86	100	70	21	14	99	85	8629	5746	41	Y	N	N	N	N
30	58	F	152	112	70	84	112	64	18	18	91	86	6681	4933	42	Y	N	N	N	N
31	43	M	156	109	72	74	63	91	26	12	94	93	8918	6354	40	Y	N	N	N	N
32	59	M	100	113	84	78	85	64	11	19	91	98	8540	5913	39	Y	N	N	N	N
33	28	M	128	140	63	72	113	74	22	15	92	93	6619	4626	38	Y	N	N	N	N
34	33	M	132	104	80	98	116	101	28	16	68	93	3804	4044	36	N	Y	N	N	N
35	31	M	62	81	76	64	106	66	23	14	64	86	1972	5116	49	N	Y	N	N	N
36	56	F	96	101	51	100	105	72	25	12	69	85	1762	4900	51	N	N	N	Y	N
37	52	F	84	133	65	99	70	118	21	14	91	92	7518	5181	39	Y	N	N	N	N
38	44	F	60	138	78	81	78	74	29	15	97	87	6209	4045	40	Y	N	N	N	N
39	52	M	92	123	64	82	120	66	13	21	99	94	5218	6309	39	Y	N	N	N	N
40	55	M	68	136	65	65	80	86	27	19	83	91	1826	5383	38	N	Y	N	N	N
41	41	F	68	110	85	60	66	80	13	16	83	96	1414	7623	50	N	N	Y	N	N
42	41	F	92	95	51	74	101	67	10	18	64	94	957	7192	58	N	N	N	N	Y
43	42	F	146	140	62	78	104	84	14	18	93	94	5705	7261	39	Y	N	N	N	N
44	35	M	126	110	64	66	99	118	19	22	93	92	7531	7857	36	Y	N	N	N	N
45	35	F	144	127	84	77	115	109	21	23	70	90	1651	7650	39	N	Y	N	N	N
46	39	F	116	96	58	88	109	64	19	17	64	94	1599	6548	47	N	Y	N	N	N
47	51	M	88	136	70	83	112	120	25	14	92	85	5413	4752	45	Y	N	N	N	N
48	23	M	104	100	82	78	105	73	13	14	77	87	1638	7093	47	N	N	Y	N	N
49	20	F	90	81	50	84	84	58	30	18	75	90	1080	6878	49	N	N	N	Y	N
50	19	M	150	122	89	68	72	78	19	16	98	92	6986	6790	42	Y	N	N	N	N
51	33	F	72	120	82	89	105	113	24	11	96	90	6450	4462	41	Y	N	N	N	N
52	20	F	108	124	78	97	63	117	18	20	99	96	7394	5428	36	Y	N	N	N	N
53	24	F	152	111	88	95	106	113	13	24	98	85	7450	6206	39	Y	N	N	N	N
54	25	M	100	121	75	83	72	101	15	15	93	87	6408	4852	38	Y	N	N	N	N
55	59	F	110	87	88	62	68	55	17	10	63	88	837	7439	47	N	Y	N	N	N
56	14	M	138	129	74	90	99	117	12	12	92	93	7455	5829	45	Y	N	N	N	N
57	60	M	154	95	76	73	117	58	30	13	74	97	1663	4252	59	N	Y	N	N	N
58	34	F	76	104	87	60	89	73	18	16	70	95	1157	6236	50	N	N	Y	N	N
59	34	F	64	83	80	72	106	58	26	11	61	96	619	4933	50	N	N	Y	N	N
60	30	F	126	88	86	92	106	79	27	16	86	97	853	5293	51	N	N	Y	N	N
61	20	F	144	86	87	68	73	80	16	15	77	97	1828	6478	57	N	N	Y	N	N
62	39	M	142	127	71	85	71	66	24	18	90	88	5414	4625	38	Y	N	N	N	N
63	34	M	78	108	55	89	104	68	12	14	90	96	5507	5891	50	Y	N	N	N	N
64	21	F	86	115	83	62	66	80	23	12	91	91	5876	5222	44	Y	N	N	N	N
65	21	F	136	120	61	82	98	70	11	13	92	94	6744	5310	43	Y	N	N	N	N
66	25	F	140	99	56	97	99	51	30	10	65	90	544	7834	48	N	N	Y	N	N
67	29	F	138	125	80	80	114	93	17	18	64	93	3039	6121	46	N	N	Y	N	N

68	27	M	78	82	80	71	106	51	19	13	80	95	1690	7211	49	N	N	Y	N	N
69	47	M	152	121	74	92	93	83	12	20	98	92	6477	7427	39	Y	N	N	N	N
70	46	F	128	100	76	92	108	113	30	24	92	90	6957	4817	38	Y	N	N	N	N
71	45	M	72	99	80	95	100	76	27	17	77	92	1821	6040	47	N	Y	N	N	N
72	44	M	76	92	67	67	73	61	27	15	67	98	1836	4309	52	N	N	N	Y	N
73	41	F	96	102	53	72	93	72	13	13	78	86	561	4093	54	N	N	Y	N	N
74	40	F	114	101	79	76	84	73	11	15	60	97	1388	4388	51	N	N	N	Y	N
75	39	F	104	107	77	92	91	80	21	17	94	98	5147	5198	44	Y	N	N	N	N
76	39	F	146	104	53	85	85	73	12	15	67	92	600	5400	50	N	N	Y	N	N
77	37	F	68	99	87	93	82	75	30	14	61	88	520	4692	51	N	N	Y	N	N
78	50	M	126	92	85	74	78	78	15	13	88	95	933	4029	55	N	N	Y	N	N
79	52	M	98	128	60	79	74	88	10	17	97	96	6647	6525	41	Y	N	N	N	N
80	20	M	126	130	73	70	112	92	23	13	99	98	8977	4874	42	Y	N	N	N	N
81	20	M	120	139	65	93	113	84	17	10	74	97	2244	7692	46	N	Y	N	N	N
82	19	M	66	99	63	84	72	53	27	13	73	90	1545	6697	49	N	N	Y	N	N
83	18	M	92	121	82	80	90	78	22	23	91	90	8904	6092	39	Y	N	N	N	N
84	17	F	66	112	71	84	64	85	29	17	98	93	6458	6995	38	Y	N	N	N	N
85	29	M	66	104	67	85	77	71	15	16	66	91	1728	7401	52	N	Y	N	N	N
86	28	M	68	87	66	74	89	92	21	18	90	94	8560	5775	50	Y	N	N	N	N
87	49	F	132	122	90	74	62	115	27	14	97	88	8935	4294	42	Y	N	N	N	N
88	48	M	124	107	69	71	61	118	18	15	99	91	6388	5999	45	Y	N	N	N	N
89	47	M	96	80	60	78	109	75	21	13	69	87	850	5831	51	N	N	Y	N	N
90	47	M	136	92	82	64	118	64	18	13	82	87	1063	4369	52	N	N	N	Y	N
91	60	F	142	109	63	95	89	90	11	13	95	85	5993	7938	45	Y	N	N	N	N
92	60	F	152	85	50	77	69	51	17	16	76	92	1744	7681	49	N	N	Y	N	N
93	34	F	160	95	52	63	114	79	27	14	71	90	1665	6263	48	N	N	N	Y	N
94	30	F	82	116	66	83	93	89	29	18	92	94	5171	6494	43	Y	N	N	N	N
95	33	M	118	137	80	65	64	101	20	14	80	90	1874	6595	46	N	N	N	Y	N
96	33	M	120	120	62	95	100	86	28	14	66	97	1881	5693	43	N	Y	N	N	N
97	34	M	122	110	62	73	105	52	25	12	80	94	1093	4508	47	N	N	Y	N	N
98	35	M	106	100	90	95	110	76	13	17	90	94	7516	6750	43	Y	N	N	N	N
99	38	F	110	126	61	89	103	83	12	24	93	89	7775	7397	36	Y	N	N	N	N
100	39	F	98	107	62	68	70	93	12	21	72	93	2664	6173	39	N	Y	N	N	N
101	28	F	146	110	76	93	104	106	25	18	92	91	7125	4664	39	Y	N	N	N	N
102	29	F	62	129	78	99	69	64	16	23	93	85	8094	6521	38	Y	N	N	N	N
103	21	F	138	100	83	62	76	78	24	15	76	86	1298	4396	50	N	N	Y	N	N
104	20	M	106	99	82	75	97	73	30	10	87	87	1244	5085	52	N	N	Y	N	N
105	40	M	74	97	65	70	84	71	10	15	60	94	1604	7023	54	N	N	Y	N	N
106	28	M	68	135	77	85	102	101	22	16	94	97	6147	7543	44	Y	N	N	N	N
107	24	M	120	110	66	79	101	69	23	14	92	92	6859	7056	41	Y	N	N	N	N
108	47	M	134	113	76	99	118	70	28	11	91	89	6257	6384	41	Y	N	N	N	N
109	53	F	78	108	90	93	111	66	18	15	90	88	8892	4052	41	Y	N	N	N	N
110	50	F	98	100	82	98	110	91	18	17	92	95	5244	5351	42	Y	N	N	N	N
111	57	F	158	138	67	65	80	130	11	11	96	88	6174	7473	46	Y	N	N	N	N
112	58	F	116	98	71	69	94	63	27	10	69	91	688	4657	49	N	N	Y	N	N
113	59	F	148	105	63	78	76	96	27	23	99	98	8498	5421	38	Y	N	N	N	N
114	50	M	138	103	61	88	89	98	23	24	92	88	7347	5326	38	Y	N	N	N	N
115	30	M	128	132	87	76	100	120	16	14	90	96	7043	4913	39	Y	N	N	N	N
116	21	F	86	138	79	94	112	102	14	13	97	94	7836	5585	40	Y	N	N	N	N
117	14	M	78	100	72	92	67	76	18	12	94	94	5342	6426	40	Y	N	N	N	N
118	18	F	132	137	78	87	114	73	25	12	93	98	6597	7881	40	Y	N	N	N	N
119	19	M	156	81	51	85	100	76	18	15	62	85	1541	4652	50	N	N	N	Y	N
120	38	F	122	83	61	67	64	54	10	17	86	93	1338	7855	50	N	N	Y	N	N
121	38	M	128	81	76	73	72	62	13	13	70	91	1389	4139	54	N	N	Y	N	N
122	43	M	144	97	51	90	69	72	13	11	63	88	664	4278	52	N	N	N	N	Y
123	43	M	60	107	86	95	116	53	18	17	61	91	502	7590	50	N	N	Y	N	N
124	46	F	66	88	60	65	77	58	30	15	71	94	1290	6817	53	N	N	Y	N	N
125	45	F	146	135	90	89	104	95	16	21	97	98	7569	4596	36	Y	N	N	N	N
126	24	M	160	127	64	60	88	106	11	18	91	90	5089	5991	39	Y	N	N	N	N
127	25	F	160	109	83	84	105	110	20	19	69	85	1965	5437	37	N	Y	N	N	N
128	55	M	104	111	67	99	120	95	19	20	96	98	5668	4665	38	Y	N	N	N	N
129	44	F	154	126	80	83	114	98	15	10	88	93	3413	4533	43	N	Y	N	N	N
130	57	M	62	90	80	86	87	78	15	14	63	90	1314	6697	47	N	Y	N	N	N
131	50	F	120	116	86	83	111	116	25	16	97	93	8834	5661	42	Y	N	N	N	N
132	49	M	102	90	80	97	75	76	21	18	66	96	1808	4382	56	N	N	Y	N	N
133	59	F	86	91	81	85	89	50	27	18	67	96	1113	4036	50	N	N	N	Y	N
134	56	M	104	84	81	79	102	55	14	11	64	90	830	4251	51	N	N	N	Y	N
135	55	F	76	98	60	65	90	58	24	13	94	85	8850	7340	52	Y	N	N	N	N
136	30	M	94	105	81	99	112	52	14	13	84	87	1205	6723	54	N	N	Y	N	N
137	21	F	120	133	60	65	91	82	24	18	91	92	5438	5978	43	Y	N	N	N	N

138	32	M	146	82	68	71	87	59	22	17	87	98	1059	6761	53	N	N	Y	N	N
139	36	F	140	116	60	77	73	78	30	18	93	85	7890	6258	36	Y	N	N	N	N
140	31	M	156	129	79	97	120	102	24	17	97	97	8572	4505	37	Y	N	N	N	N
141	20	M	152	111	86	67	88	86	15	20	96	93	6015	6279	38	Y	N	N	N	N
142	25	M	98	102	76	63	61	99	13	18	99	97	5020	5458	36	Y	N	N	N	N
143	26	M	120	132	69	83	94	96	19	22	96	92	8958	6469	39	Y	N	N	N	N
144	29	M	70	116	81	74	61	93	12	24	90	98	7372	4034	38	Y	N	N	N	N
145	38	M	156	127	68	75	64	60	23	15	99	95	8832	7302	37	Y	N	N	N	N
146	34	F	68	83	77	82	113	57	23	14	76	90	1556	6331	47	N	N	Y	N	N
147	46	F	126	87	68	77	94	120	21	14	94	86	7210	7532	48	Y	N	N	N	N
148	49	F	142	84	52	74	66	112	16	12	90	95	8171	4318	49	Y	N	N	N	N
149	21	M	116	135	66	83	116	91	19	12	94	95	5611	4181	41	Y	N	N	N	N
150	47	M	118	135	76	62	61	69	20	18	95	90	5587	6734	42	Y	N	N	N	N
151	58	M	70	107	77	66	83	61	17	12	65	97	659	6956	49	N	Y	N	N	N
152	51	F	144	98	58	65	95	70	29	14	74	95	550	7025	49	N	N	N	N	Y
153	21	M	158	87	50	81	65	79	10	18	85	89	916	7838	47	N	Y	N	N	N
154	25	F	94	132	62	62	78	89	22	10	98	88	5028	5388	42	Y	N	N	N	N
155	40	M	90	108	65	75	94	73	16	15	99	95	7836	4257	40	Y	N	N	N	N
156	46	F	114	103	87	100	118	60	21	16	65	98	1532	7978	49	N	N	N	Y	N
157	49	M	134	88	88	88	91	68	10	15	84	96	1614	6713	50	N	N	N	Y	N
158	44	F	102	110	69	73	114	68	21	16	94	95	6873	5751	37	Y	N	N	N	N
159	58	M	116	81	64	93	75	80	20	18	80	93	1311	4788	50	N	N	N	N	Y
160	59	F	88	110	54	77	66	54	23	17	69	85	807	5398	51	N	Y	N	N	N
161	36	M	60	102	62	71	119	58	18	11	65	97	1375	7957	52	N	N	N	Y	N
162	52	F	152	110	78	69	113	105	17	15	91	90	8895	6835	36	Y	N	N	N	N
163	21	M	122	102	59	65	105	66	23	11	71	98	1969	5885	53	N	N	Y	N	N
164	20	F	68	89	52	74	97	65	23	13	86	91	646	7264	52	N	N	Y	N	N
165	23	M	108	108	87	98	73	72	27	22	95	85	7838	7947	39	Y	N	N	N	N
166	60	F	100	125	72	72	72	63	27	16	94	97	5372	4967	38	Y	N	N	N	N
167	55	M	76	137	73	83	77	84	24	16	91	97	8638	5589	36	Y	N	N	N	N
168	20	F	114	122	62	67	101	76	23	18	92	90	7990	6267	39	Y	N	N	N	N
169	24	M	132	114	61	83	93	103	11	11	92	98	6676	7022	42	Y	N	N	N	N
170	42	M	114	102	53	99	104	53	12	18	62	95	1617	5731	50	N	Y	N	N	N
171	42	M	114	106	78	73	72	92	10	18	95	96	6333	4115	40	Y	N	N	N	N
172	42	M	160	86	58	83	94	75	15	18	85	95	1308	5435	54	N	N	Y	N	N
173	45	M	86	87	67	85	120	72	16	15	76	95	920	6046	54	N	N	Y	N	N
174	46	F	102	94	56	82	62	61	28	13	85	91	1065	4358	54	N	N	Y	N	N
175	36	F	104	87	83	67	78	67	27	10	66	91	1545	7643	56	N	N	Y	N	N
176	39	F	98	110	64	77	64	59	27	17	72	87	1712	5982	56	N	N	Y	N	N
177	30	M	128	103	66	82	73	61	24	15	81	93	543	6063	51	N	N	Y	N	N
178	21	F	90	110	78	71	96	72	29	14	93	97	7591	5162	42	Y	N	N	N	N
179	36	M	142	112	61	89	113	103	13	16	79	85	2315	5609	46	N	Y	N	N	N
180	33	M	114	106	84	97	88	94	26	16	94	87	6555	7575	45	Y	N	N	N	N
181	30	F	118	115	61	85	100	93	21	16	70	91	2037	7715	46	N	N	Y	N	N
182	20	M	150	102	64	98	61	54	17	17	76	85	1006	4538	49	N	N	N	Y	N
183	60	F	62	134	76	63	51	82	15	16	85	88	2747	7444	38	N	Y	N	N	N
184	50	M	118	121	65	62	104	64	23	24	94	93	5882	6330	39	Y	N	N	N	N
185	40	F	140	107	70	77	85	119	23	24	97	95	8954	6912	37	Y	N	N	N	N
186	40	M	156	103	64	60	83	83	18	17	90	86	5030	6305	38	Y	N	N	N	N
187	40	M	120	123	85	74	94	110	24	16	92	88	7399	6013	46	Y	N	N	N	N
188	50	F	142	85	69	64	95	52	26	14	61	89	1230	7031	49	N	N	N	Y	N
189	20	M	130	111	67	89	104	90	20	11	90	87	8005	6594	42	Y	N	N	N	N
190	31	M	150	91	88	67	102	70	14	18	73	86	705	5178	48	N	Y	N	N	N
191	33	F	76	131	74	90	100	108	26	12	99	87	5124	4072	42	Y	N	N	N	N
192	59	M	148	91	76	80	68	57	15	13	87	93	824	6968	49	N	N	N	Y	N
193	19	F	76	82	90	74	118	74	26	18	82	87	1258	7175	49	N	N	Y	N	N
194	15	M	112	129	74	99	115	88	13	10	96	86	7155	7978	45	Y	N	N	N	N
195	18	M	122	84	70	93	88	53	30	17	61	91	1132	5251	47	N	N	Y	N	N
196	16	F	156	116	74	74	69	75	30	16	83	92	725	7277	47	N	Y	N	N	N
197	19	M	112	83	70	66	107	60	10	17	78	90	1922	5124	49	N	Y	N	N	N
198	17	F	68	80	76	72	79	76	17	18	72	85	1900	6254	49	N	N	N	Y	N
199	19	F	96	86	74	90	105	67	21	17	84	86	1426	6132	55	N	N	N	N	Y
200	39	M	80	94	80	91	73	51	27	16	77	94	593	7939	52	N	N	Y	N	N

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Period of Study	:	2016-2019
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